THE DEUTERIUM ISOTOPE EFFECT

IN

AROMATIC SULPHONATION

by

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C O N T E N T S

INTRODUCTION

Discovery and Isolation of Deuterium

After the discovery that oxygen contained small quantities of the isotopes ^{17}O and ^{18}O (1) in order to account for anomalies in the experimental atomic weights it was postulated by Birge and Menzel (2) that hydrogen must contain 1/4,500 parts of an isotope of mass 2. At that time, however, the existence of the isotope had not been demonstrated experimentally. In 1932, Urey, Brickwedde and Murphy (3) succeeded in concentrating deuterium by fractional distillation of liquid hydrogen near its triple point, and they showed by spectroscopic methods that the heavy isotope was present in ordinary hydrogen and to a greater extent in the sample which had been enriched by distillation. The discovery of deuterium was confirmed by Bleakney using the Mass Spectrograph (4).

Following the discovery and concentration of deuterium a considerable amount of research was carried out to find a method of obtaining a pure sample; fractional distillation (3), gas diffusion (5) and differential adsorption on catalysts (6) were among the many processes investigated for this purpose, but the heavy isotope could not be obtained pure or in large quantities by any of these methods. It was not until Washburn (7) discovered that it was possible to separate deuterium from hydrogen by electrolysis that pure deuterium oxide was finally isolated (8). The discovery of the electrolytic method for the concentration of "heavy water" has made it possible to obtain deuterium oxide of purity

greater than 99%, cheaply and in quantity for isotopic studies.

The Deuterium Isotope Effect.

Before enough deuterium was available for experimental investigation of its properties, it was predicted by various workers that there would be marked differences in the chemical behaviour of hydrogen and deuterium. Urey and Rittenberg (9) using statistical methods calculated the equilibrium constants of hydrogen-deuterium exchange reactions, and Cremer and Polyani (10) suggested that the two isotopes would react at different rates due to zero-point energy differences.

Several factors contribute to the difference in chemical reactivity of bonds to deuterium and bonds to hydrogen.

(i) Tunnel Effect. According to classical mechanics a particle must have energy equal to or greater than the energy of activation before it can surmount the potential barrier, but it can be shown by quantum mechanics that there is a definite probability that molecules with energy less than the activation energy will succeed in getting from the initial to the final state. Since it is considered energetically impossible that such particles can go over the energy barrier it is suggested that they go through the energy barrier. This effect is, therefore, known as tunnelling . The smaller the mass of a particle the greater is its deviation from classical behaviour, and, as a result, the tunnel effect will be more pronounced for reactions involving

proton transfer than for these involving deuteron transfer. This should lead to the reaction rate for hydrogen compounds being greater than for the corresponding deuterium compounds. Bell and Caldin (11) have found that the influence of tunneling on the hydrogen isotope effect is negligible at normal temperatures, but at lower temperatures this factor becomes more important (12).

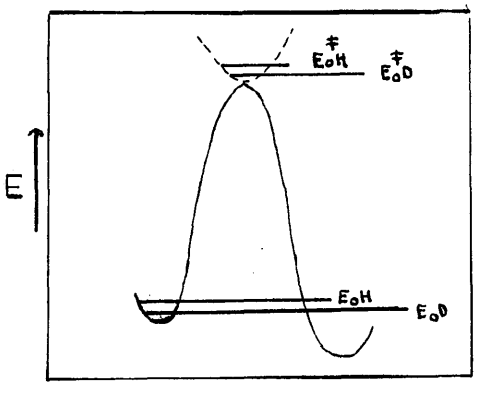
(ii) Effect of Mass. The difference in mass will affect the velocity of passage over the potential energy barrier, but in most reactions the hydrogen or deuterium atom forms part of a much heavier molecule and this mass effect can be neglected.

(iii) Zero-point Energy Difference. The most important factor is the difference in zero-point energy of hydrogen and deuterium compounds. According to quantum theory the energy of a vibrating system can never fall to zero. Even at absolute zero each vibration will have the energy $\frac{1}{2}h\nu_i$, where h represents Planck's constant and ν_i is the frequency of vibration. Since the next possible energy level has the energy $\frac{3}{2}h\nu_i$, and the energy difference $h\nu_i$ usually amounts to several kcal. per mole, almost all the molecules present in the system will have the zero-point energy $\frac{1}{2}h\nu_i$.

The potential energy curves for a hydrogen compound to a deuterium compound are identical (Fig.1), but owing to the mass difference the vibrations of the hydrogen compound will have a higher frequency than those of the deuterium compound. The zero-point energy $E_{o,H}$ of the

hydrogen compound will, therefore, be greater and the molecules containing hydrogen will possess more energy than those containing deuterium. As a result in a rate process the deuterium compound will require a greater energy of activation to surmount the energy barrier.

Fig. 1



If in the activated complex the hydrogen is tightly bound, the difference in zero-point energy between protium and deuterium in the activated complex will partly cancel out the initial zero-point energy difference. As the strength of the bonding in the activated complex decreases the isotope effect will increase.

The theoretical value of the deuterium isotope effect can be calculated from the Theory of Absolute Reaction Rates (13,14). This theory assumes that the first step in any reaction is the formation of an activated complex, the energy of activation being the difference in energy of the complex and the reactants. The activated complex has all the properties of a stable molecule except in one mode of vibration;

movement in this direction leads to decomposition. Using the various assumptions on which the theory is based it is possible to arrive at the equation,

$$k = \kappa \frac{C^{\ddagger}}{C_A C_B} \left(\frac{kT}{2\pi m^*} \right)^{\frac{1}{2}} \frac{1}{\delta} \qquad \ldots\ldots 1.$$

where k is the rate constant, κ is the transmission coefficient, δ is the length of the top of the potential energy barrier, m^* is the effective reduced mass of the complex along the coordinate of decomposition, k is the Boltzman constant, T is the absolute temperature, $C^{\ddagger}$ is the concentration of activated complex, and C_A and C_B are the concentrations of the reactants. Assuming B to be a common reactant the ratio of the rate constants for a protium compound, A_1 and its deuterium analogue, A_2, will be,

$$\frac{k_1}{k_2} = \frac{\kappa_1 C_1^{\ddagger}}{\kappa_2 C_2^{\ddagger}} \frac{CA_2}{CA_1} \left(\frac{m_2^*}{m_1^*} \right)^{\frac{1}{2}} \frac{\delta_2}{\delta_1} \qquad \ldots\ldots 2.$$

There is very little difference in the values of the transmission coefficients for systems involving hydrogen and deuterium atoms (16), ie. $\kappa_1 = \kappa_2$ and since isotopic molecules have almost identical potential energy surfaces $\delta_1 = \delta_2$ therefore,

$$\frac{k_1}{k_2} = \frac{C_1^{\ddagger}}{C_2^{\ddagger}} \frac{CA_2}{CA_1} \left(\frac{m_2^*}{m_1^*} \right)^{\frac{1}{2}} \qquad \ldots\ldots 3.$$

The concentration terms may be replaced by the corresponding complete partition functions, hence

$$\frac{k_1}{k_2} = \frac{Q_1^{\ddagger}}{Q_2^{\ddagger}} \cdot \frac{QA_2}{QA_1} \left(\frac{m_2^*}{m_1^*} \right)^{\frac{1}{2}} \qquad \ldots\ldots 4$$

The complete partition function Q is to a first approximation the product of the translational, rotational and vibrational partition functions. Since the above ratio involves isotopic molecules, the translational and rotational factors will cancel and the ratio of the complete partition functions can be expressed as a simple function of the vibrational energy levels of the two molecules (15),

$$\frac{k_1}{k_2} = \frac{f}{f^{\ddagger}} \left(\frac{m_2^*}{m_1^*} \right)^{\frac{1}{2}} \qquad \ldots\ldots 5$$

where the function f is given by the equation

$$f = \frac{s_1}{s_2} \prod_{i}^{3n-6} \frac{u_i}{u_i + \Delta u_i} e^{\Delta u_i/2} \frac{1 - e^{-(u_i + \Delta u_i)}}{1 - e^{-u_i}} \qquad \ldots\ldots 6$$

s_1 and s_2 are the symmetry numbers, $u_i = h\nu_i/kT$ and $\Delta u_i = h/kT(\nu_i 1 - \nu_i 2)$. There is a similar expression for $f^{\ddagger}$. In order to simplify the calculation it is assumed that non-reacting bonds do not change their character during the reaction, and that it is only necessary to consider the longitudinal vibrational frequency of the reacting bond. Since there is so little known about the energy levels of the activated complex, it is usually possible to determine only the maximum isotope effect. In this case there is no bonding in the activated complex and $f^{\ddagger} = 1$, therefore,

$$\frac{k_H}{k_D} = \left(\frac{m_D^*}{m_H^*}\right)^{1/2} \frac{h\nu_D}{h\nu_H} e^{(h\nu_H - h\nu_D)/2RT} \quad \frac{1 - e^{-h\nu_H/RT}}{1 - e^{-h\nu_D/RT}} \qquad \ldots\ldots 7$$

where hν is expressed in calories per mole, $\frac{1 - e^{-h\nu_H/RT}}{1 - e^{-h\nu_D/RT}} = 1$ up to about 500°C, the ratio $h\nu_D/h\nu_H$, of the vibrational frequencies for a bond to hydrogen and a bond to deuterium is approximately equal to $1/\sqrt{2}$ in most cases, this will cancel the mass factor, (m_D^*/m_H^*), which is approximately equal to $\sqrt{2}$. Therefore, the equation for the maximum isotope effect may be written,

$$\frac{k_H}{k_D} = e^{(h\nu_H - h\nu_D)/2RT} \qquad \ldots\ldots 8$$

It is necessary to apply a correction to equation 8 to account for the tunnel effect. At ordinary temperatures, however, this correction will be negligible (11).

PART I.

INVESTIGATION OF THE SOLUTE ISOTOPE EFFECT IN ELECTROPHILIC AROMATIC SULPHONATION.

Electrophilic Aromatic Substitution Reactions.

The replacement of hydrogen in an organic molecule by another atom or group of atoms is generally termed substitution.

Early in the present century Holleman (17) showed that in aromatic substitution reactions the position of substitution is influenced by the substituents already present in the ring. These orientation effects have since been investigated thoroughly by Ingold et al., and it is from these investigations that the Electronic Theory of Organic Chemistry has developed. At the present time the nature of the effects governing the position of substitution have been elucidated but there is still much to be learned of the mechanism of substitution.

According to the classification of the "English School" substitution reactions are of two main types, homolytic and heterolytic. In a homolytic reaction the attacking agent takes over one electron of the original bond; in a heterolytic reaction it takes over none or both electrons of the original bond, the former being termed nucleophilic substitution and the latter electrophilic. It has been established that the common aromatic substitution reactions nitration, halogenation, sulphonation and azo-coupling are electrophilic in character.

The purpose of the present work has been to elucidate further

the mechanism of aromatic sulphonation, in oleum.. It is not possible to interpret fully the results of this study without reference to the previous investigations, especially nitration, from which our knowledge of the mechanism of electrophilic aromatic substitution has been derived.

Aromatic Nitration.

Until 1946, the exact nature of the attacking agent in aromatic nitration had not been established. It was postulated by several workers that the active species was the NO_2^+ ion and a considerable amount of indirect evidence accumulated to favour this assumption (18,19,20, 21). Conclusive evidence was finally obtained from kinetic investigations of nitration rates in organic solvents, especially nitromethane and acetic acid. Benford and Ingold (22) showed that, if nitric acid was present in large excess, the nitration of benzene in nitromethane solution was a zero-order reaction. The nitration of toluene and ethyl benzene were also found to be zero-order and to have the same rate constant as benzene. This independence of the concentration and even the nature of the aromatic compound indicates that in these reactions the aromatic compound is not involved in the rate-determining stage. Since the same zero-order kinetics have been found for the nitration of toluene, xylene, mesitylene and ethyl benzene in acetic acid, it is obvious that the slow process cannot be specific to the solvent. Hughes, Ingold and Reed (23) have established that the slow step is in fact the formation of the nitronium ion

according to the scheme:

$$HNO_3 + HNO_3 \rightleftharpoons H_2NO_3^+ + NO_3^-$$

$$H_2NO_3^+ \rightleftharpoons H_2O + NO_2^+ \quad \text{.....1.}$$

$$NO_2^+ + ArH \longrightarrow ArNO_2 + H^+$$

Several tests of this mechanism are possible. It is obvious that nitronium ion formation will be rate controlling only if the nitronium ions react with the aromatic compound more rapidly than they recombine with water. If the aromatic compound is sufficiently unreactive, it is possible that the rate of the forward reaction of the third stage may be equal to or less than the rate of the reverse reaction of the second stage, and since the aromatic compound will then be involved in the rate determining stage one would expect the rate of reaction to be dependent upon its concentration. With monohalobenzenes it has been shown that the reaction is between zero- and first order with regard to the aromatic compound, and with still less reactive compounds eg. dichloro- and trichlorobenzenes it has been found that the nitration rate in acetic acid is definitely first order.

Although the nitronium ion has been found to be the active species in the reactions which have been investigated, it is not necessarily the nitrating agent in all cases, and it is believed that under certain conditions nitronium ion donors such as $H_2O.NO_2^+$, $AcO.NO_2$, N_2O_5, and HNO_3

may be responsible for nitration.

Mechanism of Attack by the Nitronium Ion.

In the attack on the aromatic ring by a nitronium ion, there are two plausible mechanisms for the replacement of a hydrogen atom by a nitro group; this may be a one stage process:

$$NO_2^+ + ArH + A^- \longrightarrow ArNO_2 + HA \quad \ldots\ldots\ldots 2$$

attack by the nitronium ion and removal of the proton occurring in a single step, or alternatively it may be a two stage process involving a definite intermediate of the type proposed by Pfeiffer and Wizinger (24):

$$ArH + NO_2^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Ar^+\!\!<^{H}_{NO_2} \qquad \ldots\ldots\ldots 3$$

$$Ar^+\!\!<^{H}_{NO_2} \xrightarrow{k_2} ArNO_2 + H^+$$

Kinetic evidence favours the second mechanism, but it is not possible to distinguish between the two mechanisms directly by kinetic methods. Proof that electrophilic aromatic nitration involves a two stage process has been obtained by the use of isotopic tracers. Melander (25,26), using tritiated aromatic compounds, found that the nitration reaction shows no isotope effect, and other workers have reached the same conclusion using (27) deuterium. These results are inconsistent with the termolecular mechanism (equation 2) since in this case the rate determining stage involves fission of a carbon-hydrogen bond and there would be an isotope effect. They are, however, consistent with a two stage mechanism of the type shown (equation 3).

For such a reaction involving a stationary intermediate,

$$\frac{d}{dt}\left[\begin{smallmatrix}+\\ Ar\end{smallmatrix}\!\!\begin{smallmatrix}H\\ \diagdown NO_2\end{smallmatrix}\right] = k_1\left[ArH\right]\left[NO_2^+\right] - k_{-1}\left[\begin{smallmatrix}+\\ Ar\end{smallmatrix}\!\!\begin{smallmatrix}H\\ \diagdown NO_2\end{smallmatrix}\right] - k_2\left[\begin{smallmatrix}+\\ Ar\end{smallmatrix}\!\!\begin{smallmatrix}H\\ \diagdown NO_2\end{smallmatrix}\right] = 0 \quad \ldots\ldots 4$$

$$\left[\begin{smallmatrix}+\\ Ar\end{smallmatrix}\!\!\begin{smallmatrix}H\\ \diagdown NO_2\end{smallmatrix}\right] = \frac{k_1}{k_{-1} + k_2}\left[ArH\right]\left[NO_2^+\right] \quad \ldots\ldots 5$$

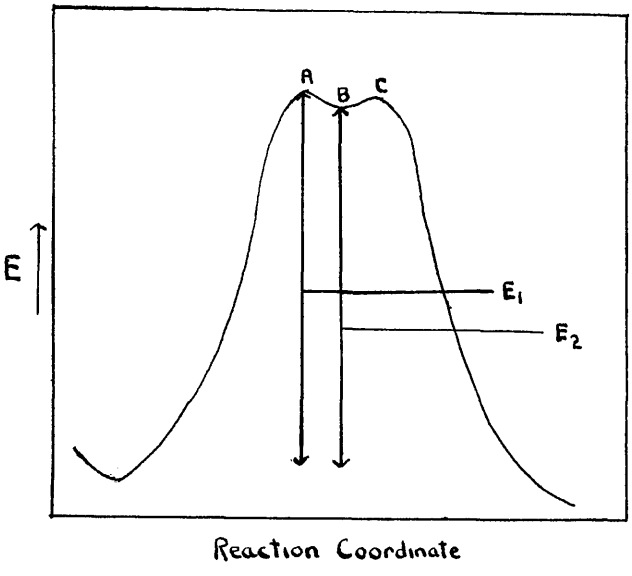
$$\text{velocity of reaction, } v = k_2\left[\begin{smallmatrix}+\\ Ar\end{smallmatrix}\!\!\begin{smallmatrix}H\\ \diagdown NO_2\end{smallmatrix}\right] = \frac{k_1 k_2}{k_{-1} + k_2}\left[ArH\right]\left[NO_2^+\right]$$

$$= \frac{k_1}{1 + \frac{k_{-1}}{k_2}}\left[ArH\right]\left[NO_2^+\right] \quad \ldots\ldots 6$$

If $k_2 \gg k_{-1}$, $v \propto k_1$, the rate of reaction will be controlled by the stage which does not involve the carbon-hydrogen bond; therefore, there will be no isotope effect. On this basis it has been concluded that nitration is a two stage process in which the attack on the aromatic ring by the electrophilic nitronium ion is rate-determining, and the subsequent loss of a proton is fast.

The conclusions have been criticised by Hammond (28). Hammond believes that if an intermediate is formed in nitration, it will most probably have the geometrical structure suggested by Ingold (see p. 14). If this intermediate has a heat of reaction E_2 (Fig. 2) similar to the activation energy E_1, it should be closely related to the transition states through which it is formed and destroyed.

Fig.2



On the potential energy diagram (Fig.2) the saddle point, B, corresponds to such an intermediate and the shoulders, A and C, to the transition states from which the intermediate is formed and through which it passes to the products. It is obvious that very little energy will be required to go from B to C. Therefore, in a highly exothermic reaction, such as the removal of a proton from the intermediate, the isotope effect might be indetectably small because only a slight weakening of the C-H bond would bring the intermediate, B, to the second transition state, C.

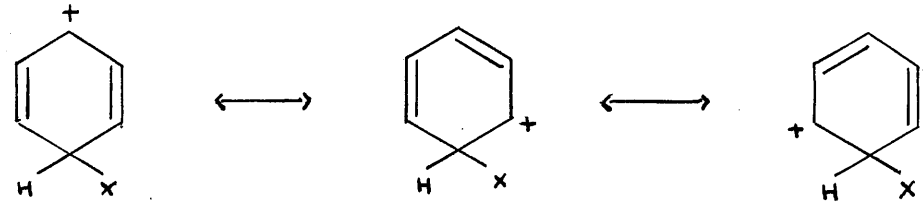
According to the above reasoning the only definite conclusion that can be drawn from Melander's results is that the breaking of the C-H bond has not made much progress in the transition state.

Evidence in favour of this theory has been obtained from an

isotopic study of the rate of removal of hydrogen from secondary (29) and tertiary amyl cations (30). Lewis and Boozer observed no isotope effect for the loss of protons or deuterons from partially deuterated secondary amyl cations; whereas in a similar but less exothermic reaction, the removal of protons or deuterons from tertiary amyl cations, a small isotope effect was observed.

Intermediate in Aromatic Substitution Reactions.

It is obviously impossible to determine the exact nature of the intermediate by normal experimental methods. A probable structure was suggested by Ingold (31) for the intermediate in aromatic nitration, and it is generally believed that the intermediates in all electrophilic aromatic substitution reactions will be of the same form:



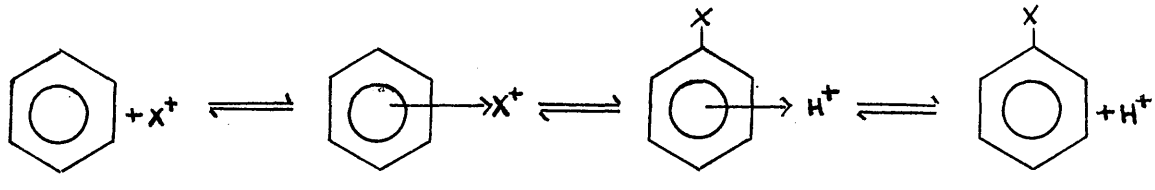
I

The proposed structure is a mesomeric cation in which two of the π-electrons of the aromatic molecule have been donated to the entering group. Both the H and the X are bound to the carbon atom by complete electron-pair bonds, and the latter atom is surrounded by four bonds of

the sp^3 type.

Dewar (32) has suggested an alternative structure to which the name π-complex has been given.

π-Complex Formation. According to the Molecular Orbital Theory of quantum mechanics, molecular orbitals do not differ essentially from atomic orbitals, in this case the electron pair occupying a molecular orbital should be available for dative bond formation as is an unshared electron pair on a single atom. Dewar considers it likely that the first stage in electrophilic aromatic substitution consists of the formation of a dative bond between the aromatic molecule and the electron deficient cation by means of the π-electrons of the former, and the empty orbitals of the latter. This bond differs from an ordinary bond only in that it links whole groups and not a pair of atoms. After bond formation the positive ion will move over the π-electron layer of the aromatic system until it eventually replaces a hydrogen by cationoid attack. The whole process is usually represented in the following manner:



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The main requirement for this type of molecular dative bond formation will be that the molecular orbital should overlap efficiently with the vacant orbital on the acceptor atom or group.

Aromatic Bromination.

Shilov and Kanjaev (33) discovered that the hypobromous acid bromination of aromatic compounds is catalysed by acids, and they established the equation,

$$-\frac{d[BrOH]}{dt} = k[ArH][BrOH][H^+] \quad \ldots\ldots 8.$$

This result has been confirmed by several workers (34,35), and it is assumed from the kinetic form of the equation that in aqueous acid the active brominating agent is either Br^+ or $BrOH_2^+$. It is not possible, however, to distinguish between these two agents. Wilson and Soper (36) showed that molecular bromine is the active species in bromination with bromine water, and this would seem also to be the case for bromination of aromatic compounds by bromine in acetic acid (37).

It has been supposed by analogy with nitration that bromination is a two step process:

$$\begin{aligned} Br^+ + ArH &\rightleftharpoons Ar^+\!\!<^{H}_{Br} \\ Ar^+\!\!<^{H}_{Br} &\longrightarrow ArBr + H^+ \end{aligned} \quad \ldots\ldots 9$$

Confirmation of this has been obtained by the use of isotopes. Using tritium, Melander (26) found that there was no isotope effect in the

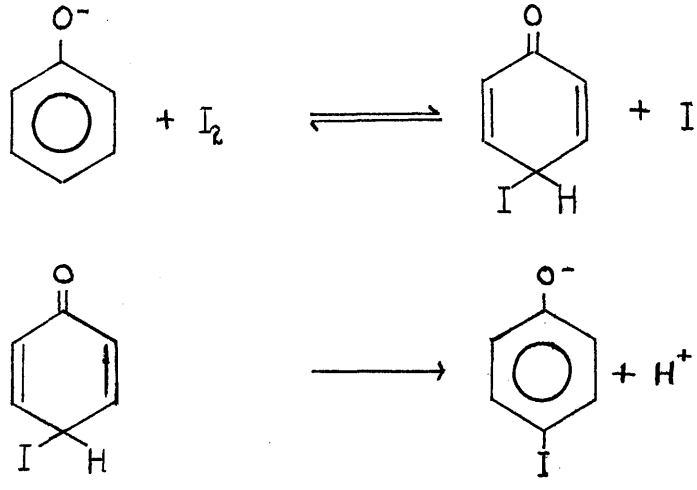
bromination of benzene and bromobenzene with iodine, ferric bromide and aluminium chloride as catalysts. These results were not conclusive since a certain amount of exchange occurred during the reaction. It has, however, been shown by de la Mare et al. (38) that in aqueous dioxan with perchloric acid as catalyst the rate of bromination of benzene and hexadeuterobenzene is identical. These results confirm what has previously been assumed, that aromatic bromination occurs in two stages, attack on the aromatic ring by the electrophilic brominating agent is rate-determining and the loss of the proton is a fast process.

Zollinger (39) has found that the bromination of 2-napthol-6:8-disulphonic acid shows an isotope effect, $k_H/k_D = 2.0 \pm 0.6$. It has been pointed out (40) that in the majority of reactions where isotope effects have been observed, the reactions have involved either phenols or amines. These are the type of compounds which would be expected to give stable intermediates and it would seem that under these conditions the intermediate must be transformed back to the reactants faster than to the products. The reaction studied by Zollinger may, therefore, be considered as a special case and the work of de la Mare and Melander is probably of more general application.

Iodination of Phenol.

A study of the kinetics of iodination of phenol in aqueous and weakly acid solutions has been made by Painter and Soper (41) and by

Berliner (42). Both groups conclude from their results that the rate-determining stage in this reaction is the attack of the phenoxide ion by I^+ or H_2OI^+ and acyl hypoiodite (or catalysis of HOI by HA). The kinetic data available do not exclude the possibility that the first stage in the reaction might be a rapid reversible attack of the phenoxide ion by the iodine molecule, followed by a rate-determining loss of a proton to the solvent or any other base present. In an attempt to distinguish between the various possibilities Grovenstein and Henderson (40) investigated the hydrogen isotope effect in this reaction and found that the rate of iodination of ordinary phenol is four times faster than the rate of iodination of 2:4:6-trideutero-phenol. The simplest interpretation of this result is that the iodination of phenol is a two stage process with the second stage rate-determining:



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If this is the case, since the iodinating agent is not involved in the rate-determining stage, it will not be possible to determine its exact

nature by the usual kinetic methods.

The Azo-Coupling Reaction.

It was established conclusively by Wistar and Bartlett (43) that the coupling reaction of diazonium compounds with aromatic amines involves attack on the free amine by the diazonium ion. Putter (44) showed that in the coupling reaction of phenols with diazonium compounds the active species are the diazonium ion and the phenoxide ion.

An intensive study of the hydrogen isotope effect in azo-coupling has been carried out by Zollinger (39) as a means of further elucidating the mechanism of the reaction.

The available kinetic data are consistent with the view that azo-coupling like other electrophilic substitution reactions is a two stage process:

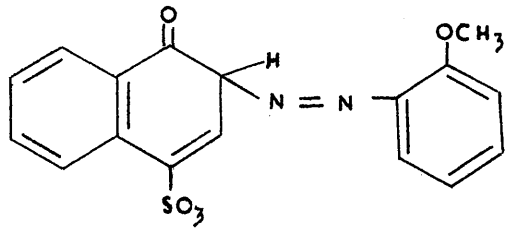
$$X^+ + ArH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Ar^+\!\!<^{X}_{H} \qquad \text{.....11}$$

$$Ar^+\!\!<^{X}_{H} + B \xrightarrow{k_2} ArX + BH^+$$

For a reaction of this type the kinetic equation can be expressed,

$$\frac{d}{dt}[ArX] = \frac{k_1 \cdot \frac{k_2}{k_{-1}}[B]}{1 + \frac{k_2}{k_{-1}}[B]}[ArH][X^+] \qquad \text{.....12}$$

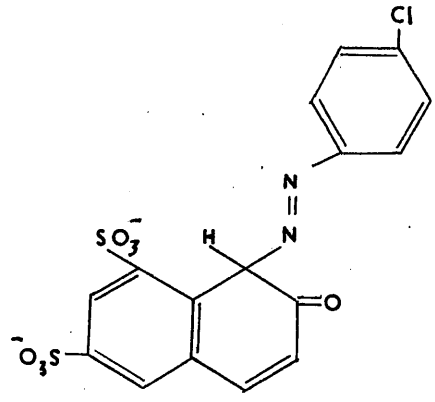
The two limiting possibilities are $k_2 \gg k_{-1}$ and $k_{-1} \gg k_2$. In the former case the velocity of the reaction, v is proportional to k_1 and there will be no isotope effect since the rate constant for the step involving fission of the carbon-hydrogen bond does not occur in the complete rate equation. In the latter case the velocity of reaction, $v = Kk_2[B][ArH][X^+]$ where $K = k_1/k_{-1}$, and since the rate constant k_2 occurs in the complete rate expression this reaction will show an isotope effect. If the above mechanism is correct it should therefore be possible by varying k_2, k_{-1} and [B] to obtain reactions showing no isotope effect, the theoretical maximum isotope effect for fission of a carbon-hydrogen bond, and isotope effects intermediate between these two extremes. Zollinger has succeeded in doing this. He has found, for example, that when 2-methoxydiazobenzene reacts with (2-^{2}H)-1-napthol-4-sulphonic acid to form II there is no isotope effect,



$$\frac{k_H}{k_D} = 1$$

II

If, however, 4-chlorodiazobenzene is coupled with (1-^{2}H)-2-napthol-6:8-disulphonic acid to form III there is a large isotope effect,



$$\frac{k_H}{k_D} = 6.55$$

III

In this reaction the experimental value of the isotope effect k_H/k_D is approximately equal to the theoretical value expected for the fission of a carbon-hydrogen bond, indicating that the second stage (equation 11) is completely rate-determining. Zollinger attributes the high experimental value of the isotope effect in this case to steric hindrance in the intermediate causing acceleration of k_{-1}. As proof of his theory he shows that when steric hindrance is reduced isotope effects intermediate between the two limiting values can be

obtained. By varying the degree of steric hindrance, the acidity of the diazo component (thus varying k_2) and the concentration of the base, Zollinger has obtained a series of values for the hydrogen isotope effect in the azo-coupling reaction. He concludes from these observations that azo-coupling, like bromination and nitration, is a two stage process.

Aromatic Sulphonation

Aromatic sulphonation has not been studied so extensively as aromatic nitration and the identity of the sulphonating agent has not yet been established completely. It would seem from the evidence available at present that the nature of the sulphonating agent is dependent upon the reaction conditions.

Hinshelwood (45,46,47) and his co-workers have studied the sulphonation of a number of aromatic compounds by sulphur trioxide in nitrobenzene solution. In all cases they found that the reaction was first order in aromatic compound and second order in sulphur trioxide. There are two possible mechanisms consistent with this kinetic data; either the sulphonating agent is the dimer S_2O_6 which is in equilibrium with the monomeric SO_3:

$$2SO_3 \rightleftharpoons S_2O_6 \qquad \text{.....13}$$

$$ArH + S_2O_6 \longrightarrow ArHS_2O_6 \longrightarrow ArSO_3H.SO_3 \rightleftharpoons ArSO_3H + SO_3$$

or the sulphonation reaction is a two stage process with the sulphur trioxide acting as sulphonating agent in the first stage and proton acceptor in the second stage:

$$ArH + SO_3 \rightleftharpoons ArH.SO_3 \qquad \text{.....14}$$

$$ArH.SO_3 + SO_3 \longrightarrow ArSO_3^- + SO_3H^+ \rightleftharpoons ArSO_3H + SO_3$$

It seems unlikely that sulphur trioxide would act as a proton acceptor under the reaction condtions, since the solvent nitrobenzene is a much stronger base and is present in large excess.

The kinetics of sulphonation of p-nitrotoluene in weak oleum have been studied by Martinsen (48) and by Cowdrey and Davies (49). Both groups obtained results showing that the reaction is first order with respect to both the aromatic compound and sulphur trioxide; in neither case, however, was any account taken of the ionisation of p-nitrotoluene. Brand (50) determined the degree of ionisation of nitrobenzene and p-nitrotoluene in the sulphonating media, and using these results he showed that the kinetics of sulphonation of nitrobenzene, p-nitrotoluene and several other organic compounds were consistent with the assumption that SO_3H^+ was the sulphonating agent in weak oleum. Brand and Horning (51,52) made a detailed study of oleum as a sulphonating medium and extended the kinetic investigations into stronger oleums. They found that if the logarithms of the experimentally

determined rate constants were plotted against the J-functions of the fuming sulphuric acids (51) straight lines with slopes slightly greater than unity were obtained; these slopes varied from 1.03 for nitrobenzene to 1.16 for the phenyltrimethylammonium ion. The correlation of log k with J eliminates SO_3 and $H_3SO_4^+$ as possible sulphonating agents and indicates that either SO_3H^+ or S_2O_6 must be the reactive species in oleum.

Melander and Larssonn (26,53,54) using tritiated benzene and bromobenzene have shown that there is an isotope effect in aromatic sulphonation. This is usually regarded as evidence that sulphonation is a two stage process with the second stage rate-determining:

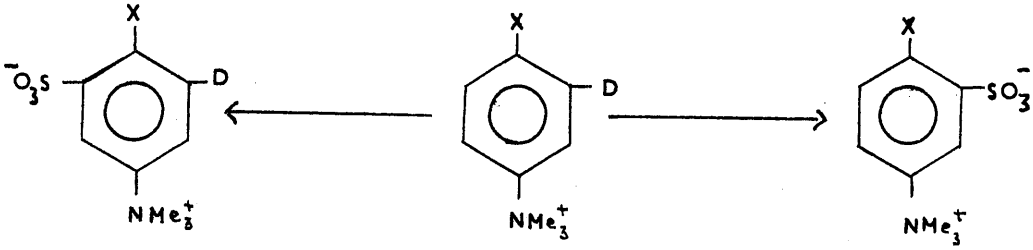
$$ArH + SO_3H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Ar^+\!\!<\!\!\begin{matrix}H\\SO_3H\end{matrix} \qquad \text{.....15}$$

$$Ar^+\!\!<\!\!\begin{matrix}H\\SO_3H\end{matrix} \overset{k_2}{\rightleftharpoons} ArSO_3H + H^+$$

The isotope effect is much smaller than would theoretically be expected for a rate-determining fission of a carbon hydrogen bond. Melander attributes this to the fact that there is not a single stationery intermediate but two forms of the intermediate in rapid acid-base equilibrium.

Nature of the Work Undertaken.

In the present series of experiments we have investigated the isotope effect in the system:



VA IV VB

where X = CH_3,F,Cl,Br

Compounds of type IV containing approximately 0.5%D were synthesised by established methods. The deuterium was introduced into the molecule either by decomposition of a Grignard compound with deuterium oxide or by hydrogen-deuterium exchange reactions. Sulphonation of the various compounds was carried out in oleum. The ratio of the rate constants k_H/k_D was obtained by the competitive method the product being analysed for deuterium content after completion of the reaction. The deuterium content is directly related to the proportion of VA and VB in the product and to the relative speeds

of displacement of the proton and deuteron.

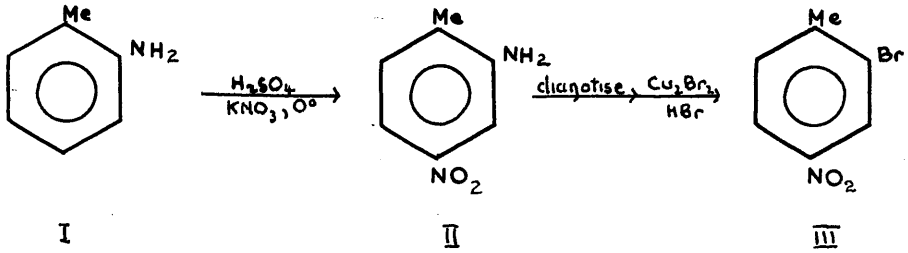
The effect of several factors on the overall rate ratio k_H/k_D was investigated.

(a) Variation of the substituent, X. Variation of X will cause a change in the electronic and steric conditions at the point of attack of the sulphonating agent.

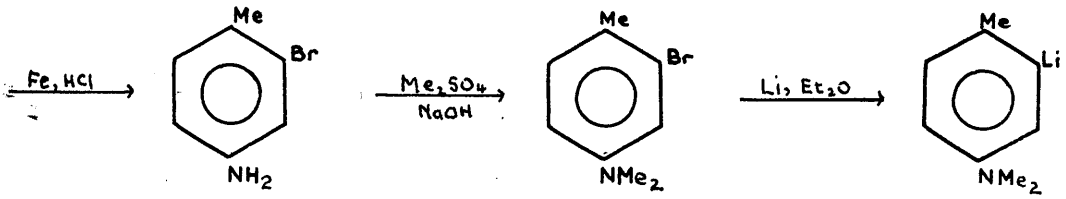
(b) Variation of the Reaction Rate. This was achieved by dissolving each compound in several oleums of different strengths. It was thought that changes (a) and (b) might alter the values of k_{-1} and k_2 (equation 15 p.24) to different extents and thus produce an experimentally observable effect on the ratio k_H/k_D.

(c) Variation of Temperature. At lower temperatures the Tunnel Effect becomes more important (12) and it was thought that this might influence the rate ratio.

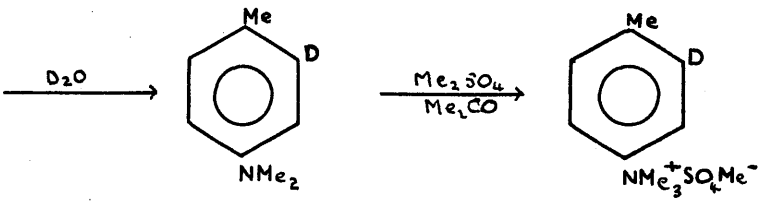
DIAGRAM 1



I II III



IV V VI



VII VIII

EXPERIMENTAL.

MATERIALS.

Preparation of (3 - ^{2}H)-4-Methylphenyltrimethylammonium Methosulphate.

The preparation was carried out as in diagram 1 p.27a; o-toluidine (I) was nitrated by the method of Cohen and Dakin (55), and the 2-amino-4-nitrotoluene (II) thus produced converted to 2-bromo-4-nitrotoluene (III) using standard Sandmeyer conditions. The nitro group of III was reduced with iron and hydrochloric acid, and the amine (IV) was methylated with methyl sulphate in the normal manner to 3-bromo-4-methyl-N:N-dimethylaniline (V). The usual precautions for the exclusion of moisture and carbon dioxide were observed in the preparation of the lithium aryl (VI). The apparatus consisted of a three necked flask fitted with a mercury sealed stirrer, a reflux condenser, closed by a silica gel tube, and a nitrogen leak. Ether (40c.c.) was added to the flask and after a short time lithium (1g.), cut to reveal fresh surfaces, was dropped into the ether. The nitrogen leak was transferred to the top of the condenser and replaced by a dropping funnel from which 3-bromo-4-methyl-N:N-dimethylaniline (12g.,0.056 mole), in ether, (15c.c.) was added drop by drop to the lithium suspension. After about ten minutes bright spots appeared on the lithium, the solution darkened, a heat of reaction was observed and the ether refluxed for a short time. Stirring was continued for 2-3 hours after the reaction had finished and the lithium compound (VI)

was then decomposed by the addition of a large excess of deuterium oxide (4g.,0.2 moles). The mixture was filtered through glass wool into a flask containing 500c.c. of water, the ether removed in vacuo and the residue steam distilled. The material obtained from the steam distillation was a mixture of unchanged starting material (V) and the product (VII), the two were separated by fractional distillation.

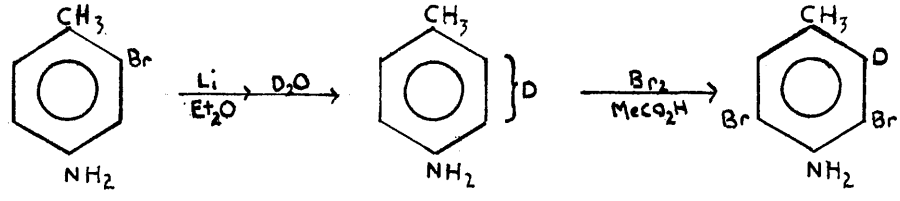
Yield 1.4g.(18%) bp 80°C/10m.m.

The quaternary salt (VIII) was prepared by reaction of the deuterated dimethylaniline (VII) with an equimolecular quantity of methyl sulphate in hot acetone solution.

m.p.144° F_D = atom % D = 0.734%

If the lithium of compound VI had been replaced quantitatively by deuterium, F_D of compound VIII would have been equal to 5.25%. Weldon and Wilson (56) have shown that, taking the normal precautions to exclude moisture, the products obtained from the decomposition of Grignard reagents by deuterium oxide are not fully deuterated. If more rigorous conditions for the exclusion of moisture are observed, fully deuterated compounds can be produced. In our case there was the possibility of contamination of the reaction mixture with protium not only from atmospheric moisture but also from the hydroxide layer on the lithium. These factors probably account for the low percentage of deuterium in the product. The deuterium content of the product was

unimportant since the isotope effect investigations were carried out by the competitive method. It was essential, however, that the deuterium should be substituted only in the position meta to the quaternary ion of compound VIII. Reactions are known (57) in which lithium preferentially replaces the hydrogen ortho to a hetero atom. It was possible, therefore, that there might be deuterium ortho to the quaternary ion of compound VIII. To establish that the deuterium was introduced only in the meta position compound IV was deuterated in the usual manner and then brominated, the aniline (IV) was preferred to the dimethylaniline (V) for this purpose, since 2:6-dibromo-4-methylaniline is a solid, easily purified by crystallisation, whereas 2:6-dibromo-4-methyl-N:N-dimethylaniline is a liquid:



IV IX X

It was calculated, that if all the deuterium of IX were present in the 3 - position the ratio $F_D(IX)/F_D(X)$ would be 1.29. The ratio found experimentally (Table 1) was 1.30 showing that there was no deuterium in the 2 - position.

Table 1. Deuterium Analysis

	log Io/I ($\lambda = 4.02\mu$)
deuterated p-toluidine (IX)	0.385
2:6-dibromo-(3-^{2}H)-4-methylaniline (X)	0.502

Preparation of (2-^{2}H)-4-nitroaniline.

The starting material used for the preparation of all the other compounds was p-nitroaniline, and the deuterium was introduced in the initial step of the synthesis by exchange. Attack on the benzene ring by the hydrogen ion is exactly the same as attack by any other electrophilic group and the same orientation rules apply. One, therefore, would expect substitution of hydrogen in p-nitroaniline, in not too strongly acid solution, to take place in the position ortho to the amino group rather than in the strongly deactivated position ortho to the nitro group.

Deuteration of p-Nitroaniline in Perchloric Acid Solution.

p-nitroaniline (2.34g., 0.017 mole) was dissolved in 15g. of 60% perchloric acid containing deuterium oxide (0.211g., 0.0105 mole). The solution contained in a glass stoppered flask was placed in a thermostat at 90°C; 1c.c. samples of the reaction mixture were withdrawn at intervals, dissolved in 10c.c. of water and the p-nitroaniline which separated was filtered, recrystallised from aqueous alcohol, dried and then analysed for deuterium content. In an exchange reaction the

deuterium content of the solute at equilibrium can be calculated approximately from the known isotopic composition of the solvent. For this reaction, after applying the correction for the deuterium consumed by the p-nitroaniline, F_D of solvent was 2.48%. If only the two hydrogens in the ortho position were replaced by deuterium, the calculated F_D of the p-nitroaniline was 0.827%. It was found that it required 5 days at 90°C. to attain isotopic equilibrium by this method (Table 2). To discover if the deuterium was being substituted only in the position ortho to the amino group of p-nitroaniline it was necessary to attain equilibrium, and for this reason the above method was inconvenient. It, therefore, was decided to substitute sulphuric acid for the perchloric acid.

Table 2. Analysis of Deuterated p-Nitroaniline.

	log Io/I ($\lambda = 4.02\mu$)	wt.% D.	Atom % D (F_D)
After 18 hours	0.186	0.48	0.43
After 90 hours	0.336	0.87	0.78
After 100 hours	0.353	0.91	0.82

(I) Deuteration of p-Nitroacetanilide in 85% Sulphuric Acid.

p-nitroacetanilide (1.84g., 0.01 mole) was dissolved in deuterated sulphuric acid (H_2SO_4 14.025 g., 0.143 mole; H_2O 2.023 g., 0.112 mole; D_2O 0.3622 g., 0.0181 mole).

The mixture, in a glass stoppered flask, was shaken for 8 hours at room temperature. The deuterated p-nitroacetanilide was subsequently hydrolysed to p-nitroaniline in the usual manner.

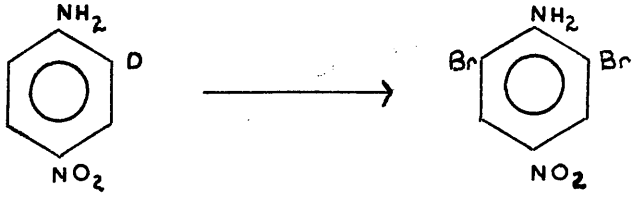
Yield 1.1g. (75%) m.p. 148°

After applying the correction for the deuterium consumed by the p-nitroacetanilide F_D of solvent was 5.24%. The theoretical deuterium percentage of the p-nitroaniline (XI), if only the two ortho positions of p-nitroacetanilide exchange with deuterium, is 1.75 atom %. Deuterium analysis of the product showed that in this reaction isotopic equilibrium had been attained. Bromination of the product confirmed that deuterium had entered almost exclusively the position ortho to the amino group (Table 3)

Bromination of p-Nitroaniline.

Deuterated p-nitroaniline (0.4g., 0.0029 mole.) was dissolved in methyl alcohol (10c.c.) and bromine (approximately 0.5c.c.) was added to the solution dropwise. The 2:6 dibromo-4-nitroaniline which precipitated was filtered off and washed thoroughly with methyl alcohol (58).

Yield 0.7g. (82%) m.p. 204°



XI XII

Table 3. Deuterium Analysis.

	log Io/I ($\lambda = 4.02\mu$)	wt.%D.	Atom %D.
deuterated p-nitroaniline (XI)	0.675	1.93	1.74
2:6-dibromo-4-nitroaniline (XII)	0.009	0.025	0.023

(II) The Deuteration of p-Nitroacetanilide in 85% Sulphuric Acid.

The preparation of deuterated p-nitroaniline was repeated several times on a larger scale (0.1 mole p-nitroaniline) to obtain sufficient starting material for the various syntheses. When the reaction was carried out on a larger scale slightly different results were obtained; equilibrium was not established within 8 hours at room temperature, and the products obtained after bromination of the deuterated p-nitroaniline still contained appreciable quantities of deuterium. The reason for the variation in the results of the pilot and preparatory experiments is unknown since the same conditions were used throughout all the experiments, the room temperature is the only factor which may have varied. A method of removing the excess deuterium in a later stage of the synthesis was found. It, therefore, was possible to use the deuterated p-nitroaniline prepared by this method to synthesise the other quaternary ammonium salts which were required.

Preparation of (3-^{2}H)-4-Halophenyltrimethylammonium Methosulphates.

Deuterated p-fluoro-, p-chloro and p-bromophenyltrimethyl-ammonium methosulphates were prepared by conventional methods as in

DIAGRAM 2

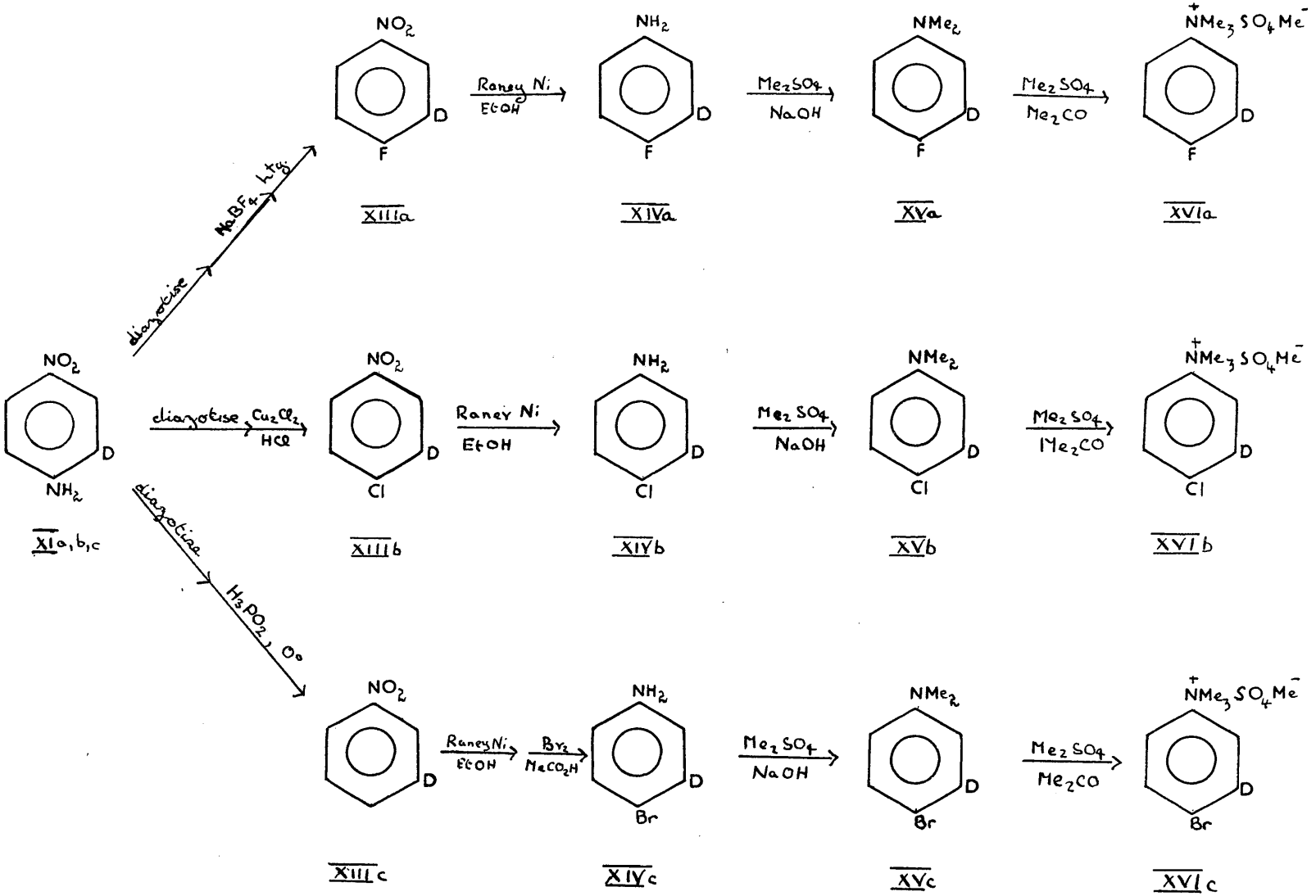
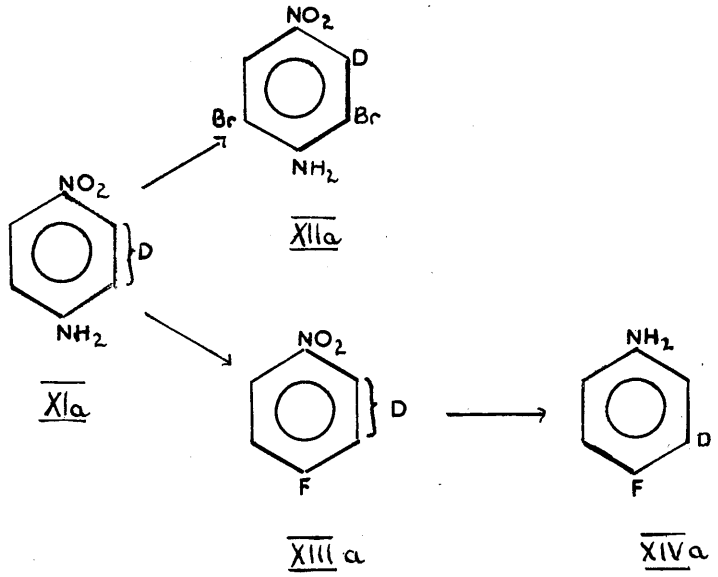

NO2
NH2
NMe2
+NMe3 SO4Me-
D
F
Cl
Br
Raney Ni
EtOH
Me2SO4
NaOH
Me2CO
diazotise
NaBF4 Heat
Cu2Cl2
HCl
H3PO2, 0°
BY2
MeCO2H
XIa,b,c
XIIIa
XIVa
XVa
XVIa
XIIIb
XIVb
XVb
XVIb
XIIIc
XIVc
XVc
XVIc

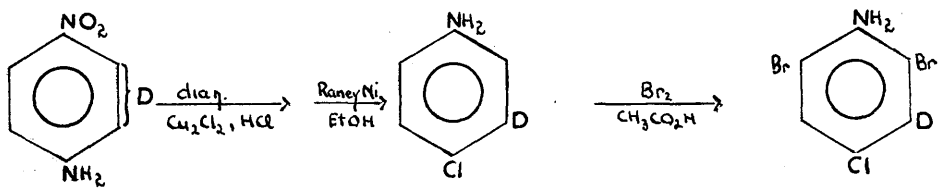
diagram 2, p.34a.

Lauer and Errede (59) have shown that Raney Nickel in sodium deuteroxide solution catalyses deuterium exchange in aniline and that 70% of the deuterium is substituted ortho to the amino group. Considering these results it was hoped not only to reduce the nitrogroup but also to remove unwanted deuterium by the use of Raney Nickel as a catalyst for the reduction of compounds XIIIa, b, c. To discover the relative amounts of deuterium in the various positions the following reactions were carried out:



The compounds XIa, XIIa, XIVa, were combusted and analysed for deuterium (Table 4). It was found that the p-fluoroaniline (XIVa) contained about 5% less deuterium than the p-nitroaniline (XIa), and analysis

of the dibromo compound (XIIa) showed that about 5% of the deuterium of XIa was in the 3 - position. These results indicate that the deuterium in the 3 - position of p-nitroaniline (XIa) was removed during its conversion to p-fluoraniline (XIVa). Rather more conclusive evidence that there was no unwanted deuterium in the reduced products (XIVa, b, c) was obtained by the following method:



XIb XIVb XVII

Analysis showed (Table 4) that the p-chloroaniline (XIVb) contained less deuterium than the p-nitroaniline (XIb) from which it had been derived, indicating that some deuterium must have been lost during the reaction. It was calculated that if all the deuterium of XIVb were present in the 3 - position the ratio $F_D(XVII)/F_D(XIVb)$ would be equal to 1.50, the experimental ratio was found to be 1.50. Considering all the evidence, it seems fairly certain that after reduction the compounds XIVa, b, c contained deuterium only in the 3 - position.

Table 4. Deuterium Analysis

	log Io/I ($\lambda = 4.02\mu$)	wt.%D	atom% D (F_D)
deuterated p-nitroaniline (XIa)	0.448	1.26	1.13
2:6-dibromo-(3-^{2}H)-4-nitroaniline (XIIa)	0.020	0.06	0.05
4-fluoro-(3-^{2}H)aniline (XIVa)	0.425	1.20	1.08
deuterated p-nitroaniline (XIb)	0.419	1.18	1.06
4-chloro-(3-^{2}H)aniline (XIVb)	0.402	1.13	1.02
2:6-dibromo-4-chloro-(3-^{2}H)aniline (XVII)	0.603	1.70	1.53

Preparation of Oleums

Potassium persulphate was added to an oleum of strength about 120% to convert any sulphur dioxide present to sulphur trioxide (sulphur dioxide will not oxidise in stronger media). Sulphur trioxide from the oleum thus treated was distilled in all glass apparatus into a known weight of AR sulphuric acid. The apparatus was then dismantled, washed with distilled water and dried in an oven at 100°C. The distillation process was repeated and a pure colourless product was obtained.

The oleums were stored in long necked flasks fitted with ground glass cones and closed with ground glass socket caps.

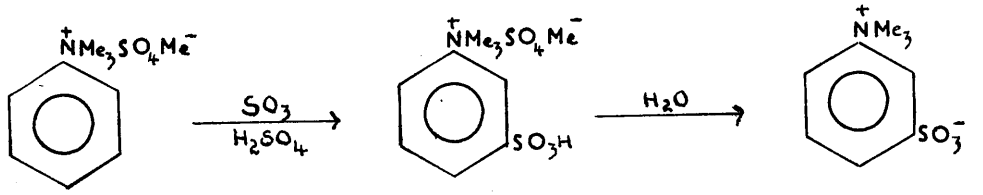
SULPHONATION

The rate of sulphonation of the aryltrimethylammonium

methosulphates in oleum is dependent upon the specific compound used, its concentration, the strength of the oleum, and the temperature of the reaction. The time for complete reaction of the several compounds studied was calculated from the velocity data of Brand and Horning (50,51).

Sulphonation of Deuterated Aryltrimethylammonium Methosulphates.

The aryltrimethylammonium methosulphate (c.= 0.5 M) was dissolved in a suitable oleum contained in a "Quickfit" flask, the flask was tightly stoppered and placed in a thermostat at 25°C for the calculated time. The oleum solution was then diluted with 20 parts of distilled water.



XVIII XIX XX

The excess acid was neutralised with AR barium carbonate (at boiling point to ensure a filterable precipitate) and filtered. After neutralisation and filtration, the filtrate contained some barium carbonate (solubility 0.1g./litre) and some soluble barium methosulphate

together with the sulphonated aryltrimethylammonium methosulphate. The solution was evaporated to small bulk (about 20c.c.) and then titrated to the pH at which all the barium methosulphate was converted to methylsulphuric acid. The required pH was calculated from the concentration of starting material. In such a strongly acid solution all the barium ions present would be converted to barium sulphate, which is almost insoluble and could be filtered off. The filtrate containing methyl sulphuric acid and the sulphonated aryltrimethylammonium compound was collected in a 50ml., B19 R.B. flask. Aromatic compounds are known to exchange their hydrogen in acid solution, to avoid this evaporation to dryness was carried out at 0°C. (Fig.3).

The residue was stirred with 2 ml. of alcohol and a crystalline material was obtained; this was filtered, washed several times with small quantities of alcohol and then recrystallised from aqueous alcohol. The isotope effects found for the sulphonation reaction are shown in Table 5.

Sulphonation of Aryltrimethylammonium Methosulphates in Deuterated Oleums.

To test that no exchange occurred during sulphonation, the undeuterated quaternary salts were sulphonated in deuterium enriched oleums. Only in the case of p-tolyltrimethylammonium methosulphate in very weak oleum was the amount of exchange of any consequence, and as the oleum strength was increased the amount of exchange decreased.

The isotope effect was investigated only in those media in which it was known that the rate of exchange was negligible.

Results are shown in Table 6.

ANALYTICAL METHODS.

Analysis of Oleums.

Oleums were analysed by the water titration method (60). A known weight of oleum (weighed to 0.01g.) was added to a glass stoppered flask and cooled to below 5°C. The cooled oleum was titrated with distilled water, added drop by drop, from a microburette. Initially a considerable amount of fume is produced in the reation, the amount diminishes until at the end-point (100% H_2SO_4) no fume whatever can be observed. The end-point is determined by the non-appearance of fume on the surface of the liquid after the flask has been cleared of fume by a puff of air. 100% sulphuric acid fumes appreciably at 13°C, it is essential, therefore, to keep the temperature near the end-point below 10°C.

Deuterium Analysis.

The deuterium analyses were carried out in the following manner. All the organic compounds were burned in a quartz combustion tube, the water produced in the combustion was collected, purified, and the deuterium content was determined by infra-red analysis.

Combustion of Deutero Organic Compounds.

The apparatus is shown in Fig. 4. The method used was a modification of the original method of Keston, Rittenberg and Schonheimer (61).

Oxygen, from a stoppered Dewar flask containing liquid oxygen, was dried by passage through sulphuric acid and through a trap at -80°C. A mercury valve prevented sulphuric acid being forced back into the liquid air if pressure inside the combustion apparatus increased. The combustion was carried out in a silica combustion tube with standard joints, Keston et al. (61) have stated that inaccurate results are obtained if rubber stoppers are substituted for the standard joints. Originally the tube was packed with a lead chromate copper oxide mixture, the purpose of the lead chromate being to remove nitrogen and sulphur oxides produced during combustion. Tubes with this type of packing had a very short life, since the lead chromate attacks the quartz at the high temperature of the furnace (700°C). It was decided, therefore, to use only copper oxide (M.A.R.) and to remove the sulphur and nitrogen oxides in the subsequent purification process. Silver gauze plugs placed at each end of the copper oxide retained any halogen combustion products. The combustion water was collected in the receiver, A.

The procedure was as follows: If the apparatus was not in continuous use, it was necessary to run it for 3 hours without a sample. Before a combustion the residual moisture was removed from the tube by

heating the exposed parts with a strong bunsen flame. Immediately after this the trap A was attached to the combustion apparatus and immersed in a freezing mixture (T = -80°C). The sample was then placed in the tube and combusted slowly. The combustion time varied from 20-40 minutes depending upon the volatility of the compound. If the compound distilled or sublimed easily, it was liable to pass through the tube without decomposing, in these cases it was necessary to carry out the combustion very slowly.

Purification of Water from the Combustion Process. The apparatus is shown in Fig.5, and is based on that used by Keston, Rittenberg, and Schonheimer (61).

A mixture of 4 parts sodium carbonate (anhydrous) to 1 part potassium permanganate was placed in the receiver, B, to remove any nitrogen and sulphur acids which were present in the combustion water. A cap was placed on B, the apparatus was evacuated and heated thoroughly with a strong bunsen flame to ensure that it was completely dry. When these prelimnaries had been completed, the combustion receiver, A, was removed from the freezing mixture, heated by hand till the ice melted and then attached to the distillation apparatus. A cap was fitted over the open end of A, the receiver, B, was immersed in an acetone-CO_2 freezing mixture and the apparatus was evacuated. A was heated gently and when all the water had distilled into B air was admitted, and the alkaline permanganate solution was refluxed for a short time with a

small flame. After B had cooled a little, vacuum distillation was continued into C. The sample was collected finally in D and transferred to a glass ampoule which was sealed awaiting estimation of deuterium oxide.

Infrared Analysis of Deuterium Oxide (62).

The intensity of the O-D stretching frequency can be measured spectrophotometrically and thus provides a method of determining the deuterium content of water samples. The purified combustion water was analysed for deuterium on a Perkin Elmer Infrared Spectrometer Model 13. Optical density measurements were carried out at the peak of the HOD fundamental at $\lambda = 4.02\mu$ using quartz cells. Each cell was made by cementing a quartz microscope slide on either side of a lead spacer. The thickness of the cell was determined by weighing empty and then full of water, 0.06 m.m. cells were used for samples containing less than 1% deuterium and 0.03 m.m. cells for samples containing 1-5% deuterium. A drop of water placed at the top edge of the cell flowed through and filled it, the cells were emptied and dried by suction. About 20 mgs. of water were required to fill the thin cells and 40 mgs. to fill the thicker cells.

The procedure for analysis was as follows: A series of standards enriched by 0-5% deuterium were prepared and a calibration curve of the optical density (log Io/I) against F_D was plotted with

water as the reference standard. The deuterium content of any sample could then be obtained by determining the optical density and reading off the F_D value from the calibration curve. In the isotope effect investigations the values of k_H/k_D were obtained merely by comparison of the optical densities of the starting materials and the sulphonated products. Values of the optical density for duplicate experiments agreed to within 1%.

When aryltrimethylammonium methosulphates were sulphonated in deuterium enriched oleums (Table 6), in every case, it was found that the product contained about 0.02 atom%D. However, when an undeuterated compound was combusted, distilled and analysed it was found to contain a similar percentage of deuterium. It is believed that, except in the case of p-tolyltrimethylammonium methosulphate in deuterated weak oleums, no exchange occurred during the sulphonation reactions and that the D_2O present in the analysed samples arose from residual deuterium present in the cells.

TABLE 5. Sulphonation of Deuterated Aryltrimethylammonium Methosulphates.

Compound	Oleum Strength $\%H_2SO_4$	$\%SO_3$	Concentration mole/Kg.	Temp.	log I_o/I	$\frac{k_H}{k_H + k_D}$	$\frac{k_H}{k_D}$
$TolNMe_3^+SO_4Me$					0.386		
$TolNMe_3^+$	102.61	11.6	0.22	25	0.310	0.634	1.73
$TolNMe_3^+$	104.99	22.2	0.27	25	0.310	0.634	1.73
$TolNMe_3^+$	102.61	11.6	0.13	0	0.316	0.647	1.83
$FPhNMe_3^+SO_4Me$					0.460		
$FPhNMe_3^+$	107.95	35.3	0.28	25	0.410	0.668	2.01
$FPhNMe_3^+$	109.62	42.7	0.25	25	0.414	0.674	2.06
$ClPhNMe_3^+SO_4Me$					0.493		
$ClPhNMe_3^+$	107.95	35.3	0.28	25	0.443	0.674	2.06
$ClPhNMe_3^+$	109.62	42.7	0.27	25	0.426	0.648	1.84
$BrPhNMe_3^+SO_4Me$					0.400		
$BrPhNMe_3^+$	107.95	35.3	0.29	25	0.353	0.663	1.97
$BrPhNMe_3^+$	109.62	42.7	0.30	25	0.350	0.656	1.91
$BrPhNMe_3^+$	109.62	42.7	0.01	25	0.355	0.665	1.99

TABLE 6. Hydrogen-Deuterium Exchange between the Solute and the Solvent during the Sulphonation Reaction

Compound	Oleum Strength $\%H_2SO_4$	Oleum Strength $\%SO_3$	F_D of Solvent	log I_o/I	F_D of Solute (calculated)	F_D of Solute (observed)
$FPhNMe_3^+$	109.02	40.1	10.8	0.021	1.20	0.019
$ClPhNMe_3^+$	109.02	40.1	10.8	0.025	1.20	0.023
$BrPhNMe_3^+$	109.02	40.1	10.8	0.023	1.20	0.021
$TolNMe_3^+$	100.47	2.09	10.5	0.100	0.93	0.090
$TolNMe_3^+$	101.02	4.53	11.1	0.042	0.99	0.038
$TolNMe_3^+$	101.45	6.45	10.6	0.025	0.94	0.023
$TolNMe_3^+$	101.80	8.00	11.4	0.020	1.01	0.018

PART II.

SOLVENT ISOTOPE EFFECT.

Introduction.

There is normally not more than 5% difference between the simple physical properties of deuterium oxide and hydrogen oxide. However, since the ionic products of the two differ by a factor of 5 (63), it is not surprising that deuterium oxide and hydrogen oxide show rather different solvent effects. A reaction may be either accelerated or retarded when deuterium oxide is substituted for water. The effect of substitution of D_2O for H_2O has been most thoroughly investigated in connection with the problems of acid-base catalysis and at one time it was thought that it would be possible to distinguish between general and specific acid catalysis by this method (64). The relationship of the solvent isotope effect, k_D/k_H, to the mechanism of catalysis is shown in Table 7.

Table 7.

Mechanism	Rate Constants	k_D/k_H
(1) $S + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} SH^+$ $SH^+ \xrightarrow[k_2]{} \text{Products}$	$k_2 \ll k_{-1}$	$\frac{k_2D}{k_2H} \cdot \frac{K_{SH^+}}{K_{SD^+}}$
(2) $S + HA \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} SH^+ + A$ $SH^+ + A^- \xrightarrow[k_2]{} X + HA$	(i) $k_2 \gg k_{-1}$ (ii) $k_2 \ll k_{-1}$	$\frac{k_1D}{k_1H}$ $\frac{k_2D}{k_2H} \cdot \frac{K_D}{K_H}$

It will be seen from Table 7 (1) that if a reaction is catalysed specifically by hydrogen ions the observed isotope effect is dependent upon the two ratios k_2D/k_2H and K_{SH}^+/K_{SD}^+. It has been shown experimentally that deutero-acids generally have smaller dissociation constants than the corresponding proto-acids, and in aqueous media the ratio K_{SH}^+/K_{SD}^+ usually lies between 2 and 3. If reaction of the conjugate acid SD^+ does not involve fission of the carbon-deuterium bond the ratio k_2D/k_2H will be approximately equal to unity and in this case one would expect the observed isotope effect to be greater than one. If, however, the second stage of the reaction does involve a rate-determining fission of a carbon-deuterium bond, the experimental isotope effect will depend upon the relative values of the ratios k_2D/k_2H and K_{SH}^+/K_{SD}^+.

In a reaction which shows the form of general acid catalysis (Table 7, (2)) the value of k_D/k_H will be governed by the relative values of the rate constants for the first and second stages of the reaction. If $k_2 \gg k_{-1}$ the observed isotope effect will be equal to the isotope effect for the first stage, k_1D/k_1H, and since the rate of transfer of a deuteron is slower than the rate of transfer of a proton the experimental isotope effect would be expected to be less than one. If $k_2 \ll k_{-1}$ the observed isotope effect will be the resultant of the two factors k_2D/k_2H and K_D/K_H, where $K = k_1/k_{-1}$, and depending upon the reaction may be greater than, less than or equal to one.

Examples can be found of reactions catalysed specifically by hydrogen ions, and by acids and bases in general (65) which show no isotope effect, isotope effects greater than one and isotope effects less than one. Due to these and various other complications it is usually impossible to derive the mechanism of catalysis merely by examination of the isotope effect. Rather more conclusive evidence regarding the nature of the catalysis can be obtained by studying the variation in the rate of reaction in H_2O - D_2O mixtures of varying composition. If a reaction is catalysed specifically by hydrogen ions:

$$S + H^+ \rightleftharpoons SH^+$$
$$SH^+ \longrightarrow \text{Products} \qquad \ldots\ldots 1$$

In a solvent containing a mole fraction n of D_2O, if the total acidity remains constant, the rate coefficient would be expected to vary with the composition of the solvent according to the equation (66,67,68),

$$k_n[S] = k_h[SH^+] + k_d[SD^+]$$
$$= k_h \frac{a_{SH^+}}{f_{SH^+}} + k_d \frac{a_{SD^+}}{f_{SD^+}} \qquad \ldots\ldots 2$$

where k_n is the velocity constant of the reaction, k_h is the specific rate constant for the SH^+ ion and k_d the specific rate constant for the SD^+ ion. K_H and K_D the thermodynamic equilibrium constants for the

proton and deuteron transfer step, respectively, can be written,

$$K_H = \frac{a_{SH^+} . a_{H_2O}}{a_S . a_{H_3O^+}} \quad \text{and} \quad K_D = \frac{a_{SD^+} . a_{D_2O}}{a_S . a_{D_3O^+}} \qquad \ldots.3$$

if the standard states are chosen so that

$$a_{H_2O} = a_{H_3O^+} = 1 \text{ in a pure protium acid}$$

$$a_{D_2O} = a_{D_3O^+} = 1 \text{ in a pure deuterium acid}$$

when these values are substituted in equation 2 then

$$k_n = k_h \frac{K_H f_S}{f_{SH^+}} \frac{a_{H_3O^+}}{a_{H_2O}} + k_d \frac{K_D f_S}{f_{SD^+}} \frac{a_{D_3O^+}}{a_{D_2O}} \qquad \ldots.4$$

It is assumed that f_S, f_{SH^+} and f_{SD^+} are independent of the isotopic composition, in which case

$$k_n = k_H \frac{a_{H_3O^+}}{a_{H_2O}} + k_D \frac{a_{D_3O^+}}{a_{D_2O}} \qquad \ldots.5$$

where k_H and k_D are the specific catalytic coefficients for 100% protium acid and 100% deuterium acid respectively. If the experimental rate of reaction is plotted against the deuterium concentration, the same type of curve should be obtained for all reactions which are catalysed specifically by hydrogen ions, since the variables in the above equation are independent of the substrate.

To test the validity of the equation Gross and his co-workers (67) examined the dependence of the rate of decomposition of

diazoacetic ester on the deuterium content of the solution, and found that the curve relating the rate of decomposition to F_D was of the form required by equation 5. They calculated the variation in activity from the distribution of picric acid between H_2O-D_2O solutions and benzene and showed that the experimental rate constant was identical with that derived from the sum of the activities using the above relationship. A large number of reactions which are known to be catalysed specifically by acids have been investigated in D_2O-H_2O mixtures, and in the majority of cases the rate of reaction has been shown to follow the above equation (65). Similar results have been obtained for the bromination of acetone (69) which is known to be a general acid catalysed reaction with the second stage rate-determining:

$$H^+ + CH_3COCH_3 \underset{k-1}{\overset{k1}{\rightleftharpoons}} CH_3\overset{+}{C}(OH)CH_3$$

$$CH_3\overset{+}{C}(OH)CH_3 + A^- \underset{k-2}{\overset{k_2}{\rightleftharpoons}} CH_3C(OH) = CH_2 + HA \quad ....6$$

$$CH_3C(OH) = CH_2 + Br_2 \xrightarrow{k_3} CH_3COCH_2Br + HBr$$

If the rate of reaction varies with the deuterium content of the solution according to equation 5, it would seem that the only conclusion which can be reached is that the reaction involves a rapid reversible protonation preceding the rate-determining stage. Although it has not been possible to make a clear distinction between general and specific acid catalysis by means of the solvent isotope effect, the effect has

been of considerable use in the elucidation of other reaction mechanisms.

Nature of the Work Undertaken.

(1) Weak oleums enriched by approximately 25%, 50%, 75% and 100%D were prepared. The effect of the deuterium content of the oleum on the acidity function, H_0 (70) was investigated.

(11) A considerable amount of kinetic evidence has accumulated to favour the assumption that in oleum the sulphonating agent is the SO_3H^+ ion which is present as a low concentration intermediate (50,51). In oleum SO_3H^+ is formed from $H_2S_2O_7$ by the following reactions:

$$HO.O_2S.O.SO_2.OH + H^+ \rightleftharpoons HO.O_2S.\overset{H^+}{O}.SO_2.OH \qquad \ldots.7$$

$$HO.O_2S.\underset{H^+}{O}.SO_2.OH \rightleftharpoons SO_2.OH^+ + HO.SO_2.OH$$

We have found that the acidity of oleum which has been enriched with deuterium is greater than that of the corresponding light oleum (Table 10). This means that the concentration of SO_3D^+ in deuterated oleum will be greater than the concentration of SO_3H^+ in a similar light oleum. If SO_3H^+ is the sulphonating agent, one, therefore, would expect the sulphonation of a protium compound to proceed faster in deuterated oleum. The kinetic data (50,51) does not exclude the possibility that SO_3 may be the sulphonating agent. In this case the rate of sulphonation would be unaffected by the deuterium content of the oleum. To distinguish between these two agents the rate of sulphonation of p-tolyl-trimethylammonium methosulphate in oleum and deuterated oleum was investigated.

EXPERIMENTAL

(1) DETERMINATION OF THE ACIDITY FUNCTIONS OF PARTIALLY AND COMPLETELY DEUTERATED OLEUMS

Hammett's Acidity Function H_o

Many chemical reactions are carried out in solutions whose acidities lie outside the range of pH measurement. To overcome this difficulty Hammett developed the acidity function, H_o, which measures acidity in terms of a basic indicator (70).

According to definition

$$H_o = -\log a_H^+ \frac{f_B}{f_{BH^+}} \qquad \ldots\ldots 8$$

It is obvious that H_o will have a definite value and be independent of the particular base used for its measurement only if f_B/f_{BH^+} has the same value for all bases in any given medium. It has been shown (71) that at least in solutions of high dielectric constant this condition is fulfilled. Hammett defines a simple basic indicator as a mono-acid base whose ionisation or salt formation is accompanied by a change in light absorbtion. From this change the ionisation ratio can be determined by colorimetric methods.

The strength of any mono-acid base is given by the quantity

$$pK_a = -\log \frac{a_{H^+} a_B}{a_{BH^+}}$$

and thus .....9.

$$H_o = pK_a + \log \frac{c_B}{c_{BH^+}}$$

Therefore, for any basic indicator, if the pK_a value is known, the H_o value can be calculated for the range of acidity over which the indicator ionises. If the H_o value of a given solution is known, the pK_a values of any indicator which ionised in that solution can be obtained similarly.

In fuming sulphuric acid mono-nitro derivatives of benzene behave as weak bases. The addition of a proton to an aromatic nitro compound causes a shift of the principal U.V. absorbtion band towards lower frequencies and increases the $\varepsilon_{max.}$ to almost twice its original value. On account of these properties, nitrobenzene and its substituted derivatives are useful bases for the evaluation of the acidity function of strongly acid solutions. By stepwise determination of the acidity function and the acidity constants of mono-, di- and tri-nitrobenzenes, Brand and Horning (52) have determined the acidity function of oleums containing 0-40% SO_3.

MATERIALS.

Preparation of Partially Deuterated Oleums.

Partially deuterated oleums enriched by approximately 73%, 48%

and 25% deuterium were prepared by dilution of strong oleums with a known weight of D_2O. The strong oleums were analysed by the water titration method (60) and the strengths of the deuterated oleums were calculated from these values. Analysis of the strong oleums was difficult due to the vigour of the reaction, and the results were only accurate to within about 3%. The strengths of the deuterated acids were later corrected using indicator data derived from protium acids, prepared from the same strong oleums. Using the values of the acidity functions obtained by Brand, Horning and Thornley (52) for these oleums, our value of the acidity constant of m-fluoronitrobenzene agree to within 0.1% with that obtained by these workers (Table 9).

Preparation of Completely Deuterated Oleums

The apparatus is shown in Fig. 6.

Completely deuterated oleums were prepared by treating a known weight of sulphur trioxide with a known weight of deuterium oxide (Norsk Hydro 99.78%). Two light oleums prepared from sulphur trioxide and water by this method were analysed conductometrically. The acid strengths derived from the conductivity data agreed to within 0.02% H_2SO_4 with these calculated from the weights.

Results are shown on Table 8.

Conductivity of Oleums.

The conductivities of the oleums were measured in a U shaped cell fitted with bright platinum electrodes. The cell was standardised with 0.1 molar potassium chloride solution. All measurements were carried out at 25°C (±0.005°), and a frequency of 3000 cycles per second, using an a.c. screened Wheatstone Bridge of the type described by Shedlovsky (72) and incorporating various modifications leading to a higher degree of accuracy.

Table 8.

Comparison of Oleum Strengths.

from Wts.	from Conductivity
$\%H_2SO_4$	$\%H_2SO_4$
100.282	100.300
100.410	100.396

Preparation of Indicator Solution.

The deuterated oleums whose H_o values were to be determined contained 6-7% sulphur trioxide. m-Fluoronitrobenzene was chosen as indicator because Brand et al (52) have shown that it is approximately one-half ionized in media of this strength.

A solution of m-fluoronitrobenzene (c.= 4.39×10^{-3}M.) was made up in AR sulphuric acid and stored in the refrigerator.

MEASUREMENTS.

To a known weight of the oleum whose H_o value was to be determined a known weight of the stock solution of m-fluoronitrobenzene was added so that the final concentration of the indicator was approximately 1×10^{-5}M. A slight correction had to be applied to the oleum strength to account for dilution by the indicator solution.

The absorbtion of the indicator in the region 2500A° to 4000A° was measured and from the observed optical densities (log Io/I) the values of the extinction coefficients, ε, were calculated. In weak oleums maximum absorbtion of the base and of the ion occurs at about 2800A° and 3400A° respectively. All the measurements were carried out on a Unicam U.V. spectrophotometer in cells with a measuring path of 1 cm., using the parent oleum as reference solvent. It has been shown by Fajans and Goodeve (73) that oleums containing less than 36% SO_3 are transparent above 2400A°.

The concentration of ion to base in the indicator solution was calculated from the relationship,

$$\frac{C_B}{C_{ion}} = \frac{\varepsilon_{ion} - \varepsilon}{\varepsilon - \varepsilon_{base}}$$

In weak oleums fairly accurate results can be obtained using the value of ε corresponding to either maximum absorbtion of the base or ion. It is preferable, however, to use the extinction coefficient of maximum absorbtion of the ion, because the change of extinction coefficient

on ionisation is twice that of the maximum of the base, and the measurements are rather more exact.

The values of ε_{ion}, ε_{base} and pK_a used to determine H_o for deuterated oleums, were those obtained by Brand, Horning and Thornley (52) Since both the deuterium oxide and the oleum had to be handled quickly, it was impossible to exactly match the strengths of the acids in the different series. To determine the influence of F_D on H_o the value of log C_B/C_{ion} at 101.6% H_2SO_4 was calculated for each acid using the relationship 1% H_2SO_4= 0.25 units H_o. The Results are shown on Table 10.

(2) KINETICS OF SULPHONATION OF p-TOLYLTRIMETHYLAMMONIUM METHOSULPHATE IN OLEUM AND DEUTERATED OLEUM.

INTRODUCTION.

The rate of sulphonation of aryltrimethylammonium methosulphates is much slower than the rate of nitration, and the sulphonated products do not nitrate. The nitrated compounds absorb strongly in the region 3000-3500A°, whereas the sulphonated compounds are transparent in this region (51). It, therefore, was possible by nitrating the unsulphonated material and measuring the light absorbtion to determine the rate of sulphonation.

MATERIALS.

The p-tolyltrimethylammonium methosulphate was prepared from N:N-dimethyl-p-toluidine and methyl sulphate in acetone. The product was recrystallised from acetone containing a few drops of water, m.p.144°.

Deuterated oleums were prepared as has been described previously (pp.53,54).

The nitrating mixture was a solution of 0.1 molar potassium nitrate in 95% sulphuric acid.

MEASUREMENTS.

The p-tolyltrimethylammonium methosulphate was sulphonated at 0°C, in oleums and deuterated oleums containing approximately 7% SO_3.

The reaction could not be carried out at 25°C since the rate of sulphonation in oleums of this strength, is too fast to be measured accurately, and weaker oleums could not be used due to the considerable hydrogen-deuterium exchange which occurs in media containing less than 4% SO_3.

The oleum (approx 3c.c.), in a weighed stoppered flask, was kept at 0°C for $\frac{3}{4}$ of an hour. A small crystal of known weight (about 0.0020g.) of p-tolyltrimethylammonium methosulphate was then added, the solution was shaken, and the reaction stopped at approximately its half-life by the addition of an excess of the nitrating medium (approx. 4c.c.).

The spectra of the reaction medium, the nitrated product in the nitrating mixture and the sulphonated product in oleum were all determined separately. It was found that the sulphonated product in oleum and the reaction medium were transparent above 2900A°, whereas the nitrated product absorbed strongly in the region 2,900A°-3,200A°. The reaction product was analysed for nitro-compound at two different wavelengths, 3000A° and 3,100A°. The optical density was proportional to the concentration of unsulphonated material and the first order rate constants could be evaluated directly. The two values obtained were averaged and the results are shown on Table 11. Since the velocity constants were measured over such a narrow range of acidity, in protium acid the values of k_H varied almost linearly with the percentage H_2SO_4. It, therefore, was possible to calculate k_H (Table 11) in those cases in which it had not been determined experimentally.

DISCUSSION.

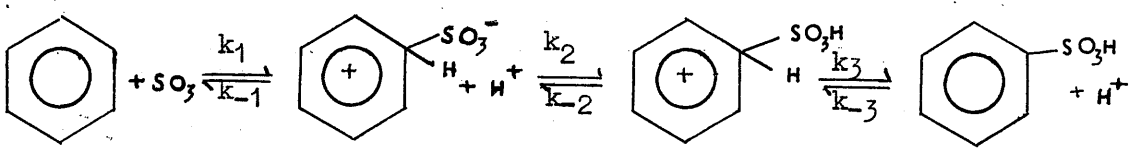
Solvent Isotope Effect.

A detailed investigation of the rate of sulphonation of aromatic compounds in oleum was carried out by Brand and Horning (51). On the basis of the evidence available these workers concluded that sulphonation could be represented most satisfactorily thus:

$$ArH + SO_3H^+ \rightleftharpoons ArSO_3H + H^+ \quad \ldots\ldots 1.$$

In the present study we have found that the acidity of oleum solutions increases linearly with deuterium content (Fig.7), and completely deuterated oleums are about 1.5 times more acidic than the corresponding light oleums (Table 10). This effect is not so pronounced as it is in aqueous media where the acidity is increased 2-3 times when hydrogen is replaced completely by deuterium. But if SO_3H^+ were the sulphonating agent, one would still expect an observable increase in the sulphonation rate on passing from light to heavy acids. We have investigated the rate of sulphonation of p-tolyltrimethylammonium methosulphate in deuterated media in which it was known that no exchange occurred, and we have found that the reaction rate in oleums enriched with 25% and 50% deuterium is identical with the rate of reaction in the corresponding protium media (Table 11). In oleums containing a higher percentage of deuterium, the rate of reaction decreases with

increasing deuterium content (Table 11). These results would not seem to be consistent with the assumption that SO_3H^+ was the sulphonating agent in oleum. If, however, one supposes that the attacking agent is not SO_3H^+ but $SO_3 + H^+$ both the observed kinetics and the isotope effect can be explained. For such a reaction the mechanism would be:



Ia Ib ..... 2.

The rate coefficients will be subject to medium effects which can be accounted for by using the Bronsted-Bjerrum relationship

$$k' = kf/f^{\ddagger} \qquad \ldots\ldots 3.$$

where k is the rate constant for the reaction in the standard state when all the activity coefficients are unity.

I_a and I_b are transient intermediates. The usual stationery state hypothesis gives,

$$d[I_a]/dt = k_1(ArH)(SO_3)/f_1^{\ddagger} - k_{-1}(I_a)/f_1^{\ddagger} - k_2(I_a)(H^+)f_2^{\ddagger} = 0 \quad \ldots 4$$

where square brackets denote concentration and parentheses denote activity.

Hence

$$(Ia) = \frac{k_1(ArH)(SO_3)}{(k_{-1}/f_1^* + k_2(H^+)/f_2^*)f_1^*} \quad \ldots\ldots 5$$

Similarly if it is assumed that the speeds of the proton loss and gain (step 2 in equation2) are very fast.

$$d[I_b]/dt = k_2(I_a)(H^+)/f_2^* - k_{-2}(I_b)/f_2^* = 0 \quad \ldots.6$$

whence,

$$(I_b) = \frac{k_2}{k_{-2}} (I_a)(H^+) \quad \ldots\ldots 7$$

We shall assume that desulphonation is of negligible importance under the conditions considered here, $k_{-3} = 0$, and so

$$v = k_3(I_b)/f_3^* = k_3 \frac{k_2}{k_{-2}} \frac{k_1(ArH)(SO_3)(H^+)}{(k_{-1}/f_1^* + k_2(H^+)/f_2^*)f_1^* f_3^*}$$

$$= k_3 \frac{k_2}{k_{-2}} \frac{k_1[ArH](SO_3)(H^+)f_{ArH}}{(k_{-1}/f_1^* + k_2(H^+)/f_2^*)f_1^* f_3^*} \quad \ldots 8$$

where v is the velocity of sulphonation. Except in special circumstances, sulphonation in fuming sulphuric acid is an apparent first-order process (50),

$$v = k_{exp.}[ArH] \quad \ldots\ldots 9$$

Combining equations 8 and 9 we get

$$k_{exp.} = k_3 \frac{k_2}{k_{-2}} (SO_3)(H^+) \frac{f_{ArH}}{f_1^{\ddagger} f_3^{\ddagger}(k_{-1}/f_1^{\ddagger} + k_2(H^+)/f_2^{\ddagger})} \quad .. \ 10$$

or,

$$\log k_{exp.} = A + \log (SO_3) - H_o + \log\left\{ \frac{f_{BH^+}}{f_B} \frac{f_{ArH}}{f_1^{\ddagger} f_3^{\ddagger}(k_{-1}/f_1^{\ddagger} + k_2(H^+)/f_2^{\ddagger})} \right\}. \quad 11$$

where $A = \log (k_3 k_2/k_{-2})$

In the expression 11 the k's are thermodynamic constants and so are independent of the medium. The dependence on the medium has in fact been shifted to the final term on the right hand side of 11. If the activity of sulphur trioxide in sulphuric acid solution is defined equal to its vapour pressure (51) and if for convenience we write

$$J = H_o - \log (P_{SO_3}) \quad .. \ 12$$

Equation 11 may be written in the form

$$\log k_{exp.} = -J + A + \log \left\{ \frac{f_{BH^+}}{f_B} \frac{f_{ArH}}{f_1^{\ddagger} f_3^{\ddagger}(k_{-1}/f_1^{\ddagger} + k_2(H^+)/f_2^{\ddagger})} \right\} \quad .. \ 13$$

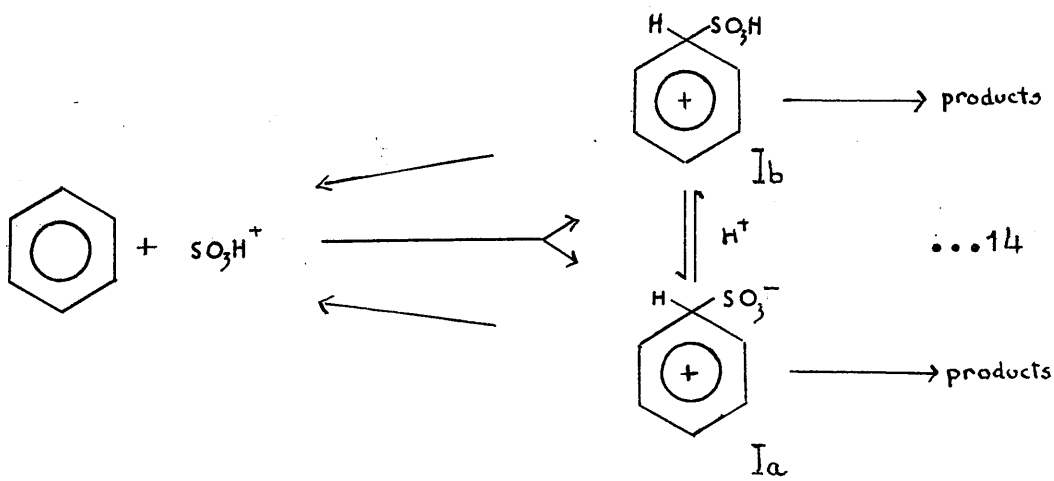
Brand and Horning (51) found that the logarithm of the experimentally rate constants varied linearly with the J function of sulphuric acid. These results are, therefore, consistent with our proposed mechanism.

The effect of the deuterium content of the solution on the rate of sulphonation will depend on the relative concentrations of I_a and I_b. If $[I_a] \gg [I_b]$ the rate of reaction would be accelerated by the acidity change when the hydrogen in the solvent was replaced by deuterium. If, however, $[I_b] \gg [I_a]$ the rate of reaction will be unaffected by the acidity of the medium though it might be expected on general grounds that the reaction would be slightly slower in the fully deuterated solvent. In oleum one would expect the intermediate to be present almost entirely as undissociated acid and, therefore, no acceleration of the rate of reaction should occur when hydrogen in the solvent is replaced by deuterium.

The above mechanism thus accounts satisfactorily for the kinetic results of Brand and Horning (51) and the experimental isotope effect (Fig.8).

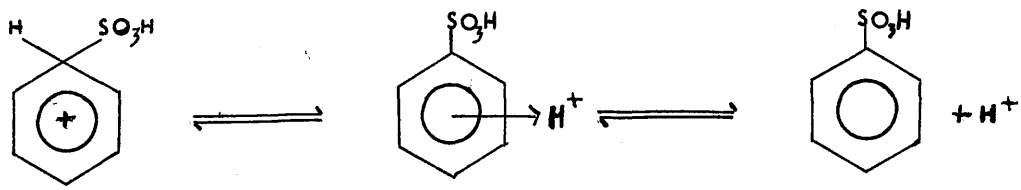
Solute Isotope Effect.

Sulphonation like other electrophilic substitution reactions is normally regarded as a two stage process (26,53). The Isotope effect observed in sulphonation reactions is usually attributed to the fact that the second stage, which involves fission of the carbon-hydrogen bond, is rate-determining. Our experimental isotope effect (Table 5) is 2-5 times smaller than would be expected theoretically if fission of the carbon hydrogen bond were completely rate-determining. Similar low results have been obtained by Melander and Larsson (53,54) for the sulphonation of tritiated benzene and bromobenzene. To explain the discrepancy between the calculated and the experimental values several theories have been advanced. Hammond (28) considers that if the intermediate is a sulphonate ion; since this would be neutral it would have unusual stability and the removal of a proton from it might involve considerable weakening of the carbon-hydrogen bond before the transition state was reached. Melander (53) believes that the low isotope effect can be explained by assuming that the second stage is only partially rate-determining, and proposes the following mechanism:



To explain the low values of the isotope effect using this mechanism, it is necessary to assume that the forward and back reactions may follow different pathways. This assumption is inconsistent with the Principle of Microscopic Reversibility.

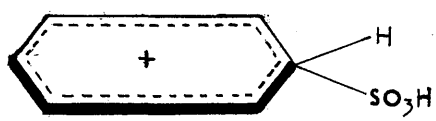
The existence of the isotope effect indicates that the proton must be involved in the slow step of the reaction. If, as Melander (53) proposes, the removal of a proton from either of the intermediates I_a or I_b were rate-determining, the rate of the reaction would be dependent upon the concentration of the base responsible for proton uptake; but unfortunately it is practically impossible to design an experiment that, in sulphuric acid solution, would establish the presence of a proton acceptor in the transition state of the reaction. A possible mechanism which explains all the observations is that the rate-determining stage involves a slow interconversion of the classical intermediate (I_b) to a π-complex (I_b''), the subsequent loss of a proton being fast:



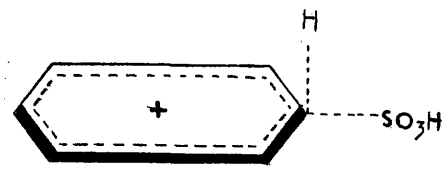
Ib Ib'' ...15

During the rearrangement from the intermediate to the π-complex the hydrogen will merely change its position, and since in the transition state it will still be bonded to the ring one would not expect a large isotope effect.

Recently an investigation of the geometry of the various intermediate stages in electrophilic aromatic substitution reactions has been carried out by Corey (74). In many cases a structure of type Ib in which the entering and leaving groups are bound by equivalent bonds has been considered as a suitable approximation of the transition state. Present kinetic data indicate (25,31,75) that I_b in fact represents a stable intermediate and corresponds to an energy minimum, whereas the transition state corresponds to an energy maximum. Corey believes that a more suitable model for the transition state is a structure in which the entering or leaving group is bonded at right angles to the ring.

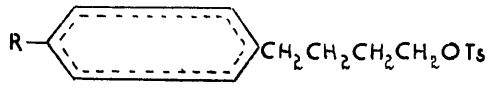


Ib

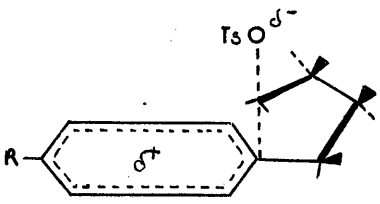


Ib'

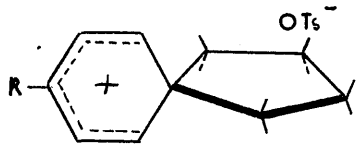
DIAGRAM 3.



II

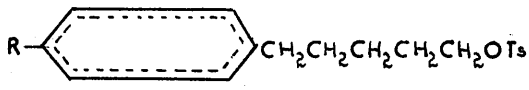


IIa

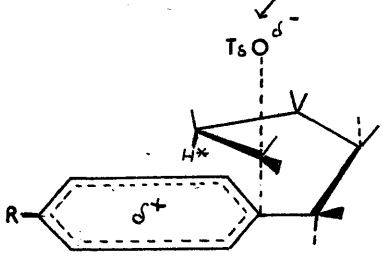


IIb

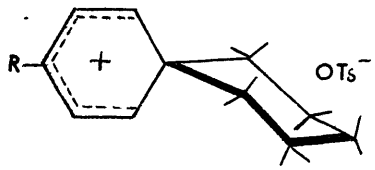
16



III



IIIa



IIIb

17

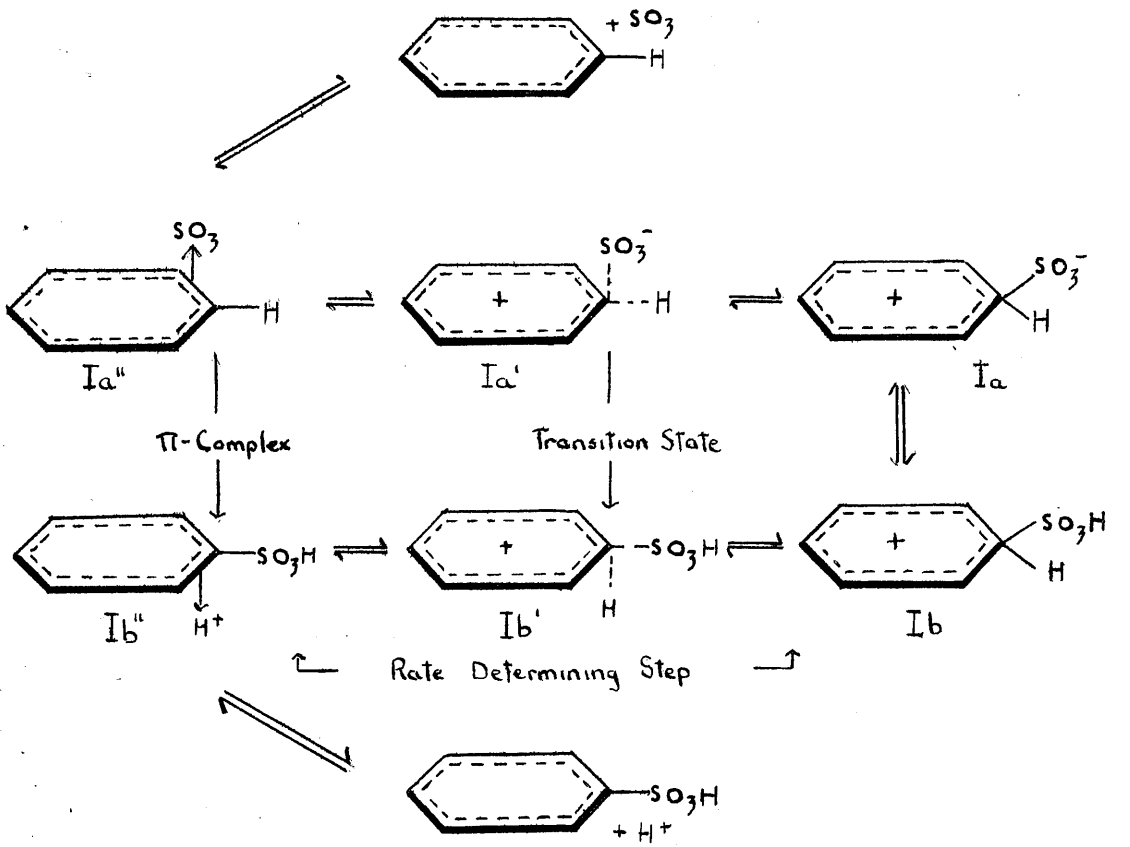
According to Corey I_b' is a better representation than I_b of the transition state of the above reaction. Evidence in favour of this supposition has been obtained from an investigation of the rate of ionisation of 4-aryl-1-butyl (II) and 5-aryl-1-pentyl (III) p-toluene sulphonates, (diagram 3, p.68a). The incipient cyclopentane ring of II_a is strainless with all the hydrogen staggered, and the linear arrangement of C_{Ar}, C_{OTs} and OTs will allow maximum participation of the aryl ring in the reaction. Structure III_a is strained due to interaction of H^* with the aryl ring, and steric hindrance will prevent the aryl group participating in the reaction. If the reactions proceeded through the transition states II_a and III_a, it would be expected that $k_{II} \gg k_{III}$ and that only the rate of reaction II would be influenced by the substituent, R.

It can be shown thermodynamically that the formation of structure II_b from II will require greater energy than the formation of structure III_b from III. It, therefore, would be expected if II_b and III_b represented the transition state that $k_{III} \gg k_{II}$.

The experimental data show that the rates of ionisation of 4-aryl-1-butyl p-toluene sulphonates are much more rapid than the rates of ionisation of the corresponding 5-aryl-1-pentyl p-toluene sulphonates, and only in the former case are the rates of reaction influenced by the substituent, R. These results indicate that the transition state must have considerably more I_b' character than I_b character.

Dewar's idea of the π-complex is a structure in which the entering or leaving group is embedded in the π-orbitals perpendicular to the benzene ring (32).

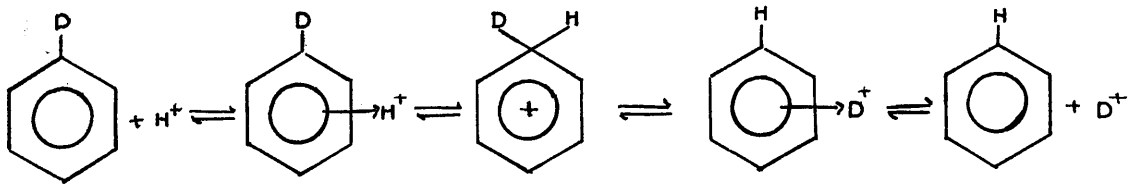
Using the various theories which have been proposed and assuming that the reaction is symmetrical, it is possible to represent the mechanism of sulphonation in detail thus:



...18

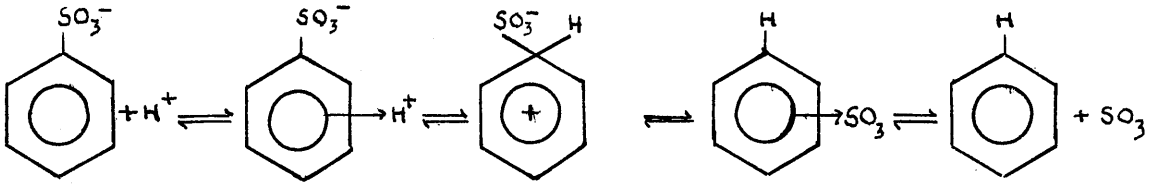
Several other workers have reached similar conslusions regarding the mechanism of electrophilic substitution of aromatic and unsaturated systems.

Gold and Satchell (76) investigated the rate of deuterium-hydrogen exchange of aromatic compounds in various aqueous acids, and found that the logarithm of the rate constant varied linearly with Hammett's acidity function, H_0. Correlation of the rate of reaction with H_0 has usually been considered as a criterion that the rate-determining step involves a conjugate acid of the substrate. In the case of the hydrogen-deuterium exchange reaction the conjugate acid SH^+ cannot be the classical intermediate (IV), because the reaction would then show the form of general rather than specific acid catalysis. It is, therefore, necessary to find a structure for the conjugate acid SH^+ such that the entering and leaving groups do not occupy equivalent positions. Gold and Satchell (76) consider that the most likely form for the conjugate acid is that of a π-complex. By analogy with nitration and other electrophilic substitution reactions it is assumed that hydrogen isotope exchange also includes a relatively stable intermediate, and the total reaction is formulated thus:



IVa IV IVb ...19

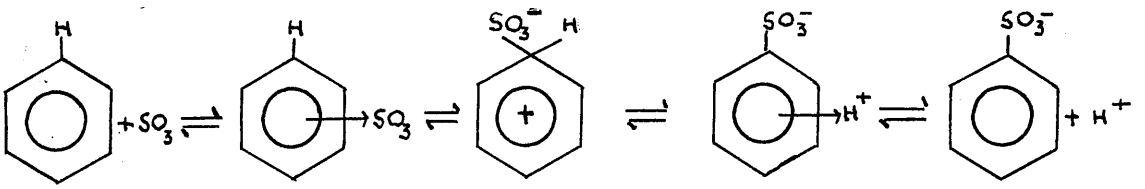
The exchange reaction involves electrophilic attack of the aromatic ring by hydrogen. If such a mechanism occurs in one case of electrophilic aromatic substitution by hydrogen it would seem likely that similar mechanisms will occur in other cases. Gold and Satchell (77), therefore, postulate the following mechanism for aromatic desulphonation:



Ic Ia Ia"

...20

It has been shown experimentally, that, in dilute aqueous acids (78), the logarithm of the rate of desulphonation follows the acidity function, H_0. In more acidic media the rate rises rather less steeply as the solvent acidity increases (79). These data are consistent with the proposed mechanism, 20. It follows from the Principle of Microscopic Reversibility that the mechanism of sulphonation will merely be a reversal of the mechanism of desulphonation:



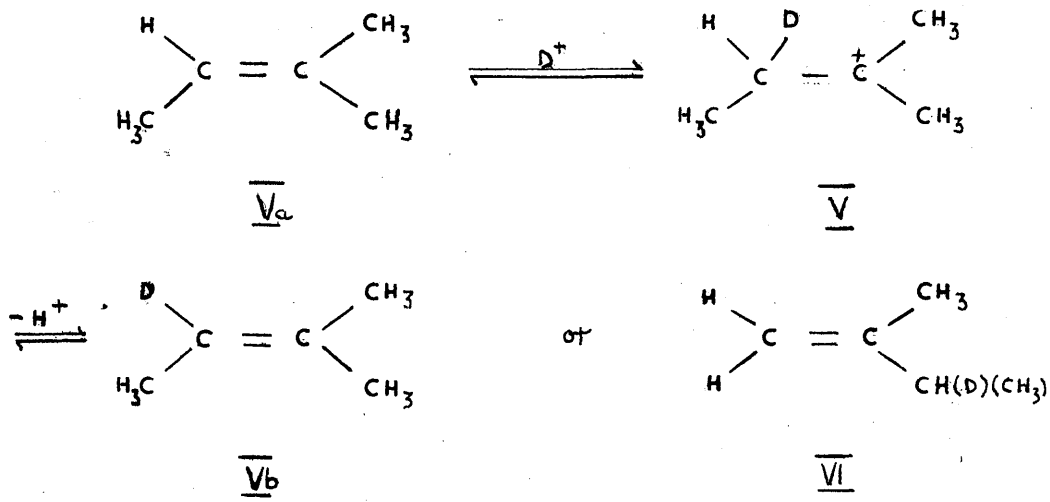
Ia" Ia Ic

...21

Gold and Satchell (77) consider the sulphonate ion to be the intermediate in aromatic sulphonation and desulphonation since it will be more reactive towards electrophilic attack than the undissociated sulphonic acid. The kinetic data, however, does not exclude the possibility that the attacking agent may be SO_3H^+, and that the intermediate may be the sulphonic acid. It seems likely that in dilute sulphuric acid the sulphonate ion will be the more important intermediate and Gold and Satchell's mechanism will operate. As the acidity of the medium increases the concentration of sulphonate ions will fall, and the concentration of sulphonic acid will rise. In solutions of high acidity one, therefore, would expect the sulphonic acid intermediate to predominate.

The idea of the rearrangement of the protonated π-complex being rate-determining was originally proposed by Taft (80) to explain the observation that the rate of hydration of butene followed Hammett's acidity function rather than the concentration of hydrogen ions. More recently Taft has studied the effect of the deuterium content of the solvent on the rates of hydration of 2-methyl-2-butene and 1-methylcyclopentene (81), and has found that the dependence of the reaction velocity on F_D follows the Nelson-Butler equation (p.49, equation 5). These results indicate that there is a reversible proton transfer preceding the rate-determining step in the hydration of olefins. When the hydration of 2-methyl-2-butene was carried out in deuterated nitric acid, the olefin removed after half time of

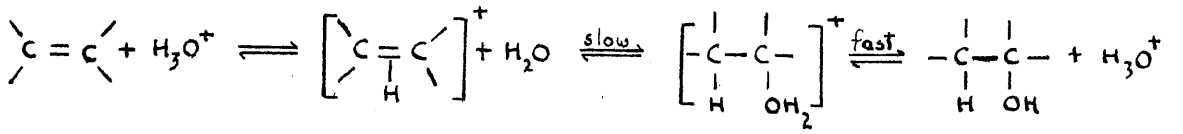
reaction did not contain a detectable amount of deuterium. The rate of transfer of a proton is faster than the rate of transfer of a deuteron. If a carbonium ion (V) were formed preceding the rate-determining step, it could be detected by the appearance of deuterium in the unreacted olefin:



...22

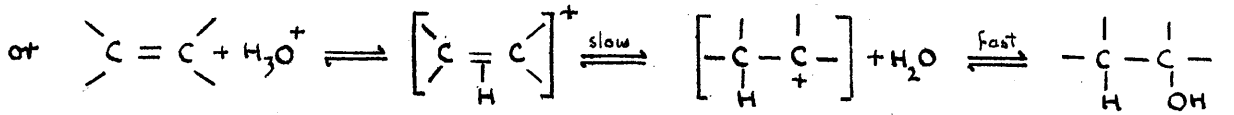
Since the conjugate acid formed in the preliminary proton transfer cannot be a carbonium ion, Taft considers the only other reasonable structure suggested by bond theory is the π-complex and that the rate-determining step in the hydration reaction involves the transfer of the hydrogen from its position in the π-complex to an adjacent carbon atom

to form a conventional C-H bond. There are two possible mechanisms consistent with the observed results,



...23

or



...24

It has been found that in the hydration of 2-methyl-2-butene and 1-methylcyclopentene, the experimental isotope effect k_H/k_D is approximately equal to one. For reactions of this type (equations 23 and 24) the observed isotope effect is the resultant of two opposing factors $k_H/k_D = (K_{SD}^+/K_{SH}^+)(k_2H/k_2D)$ where K_{SH}^+ and K_{SD}^+ are the dissociation constants of the conjugate acids formed in the first stage of the reaction. When D is substituted for H, the first stage of the reaction is accelerated and the second stage is retarded. Normally in aqueous media the ratio K_{SH}^+/K_{SD}^+ lies between 2 and 3. To account for the observed k_H/k_D ratios of unity it is necessary to assume that the isotope effect for the rate-determining stage k_2H/k_2D has a similar value. These results would seem to be consistent with our own.

We have proposed a rate-determining proton transfer for the sulphonation reaction and have found an isotope effect of approximately 2.

TABLE 9. Acidity Constant of m-Fluoronitrobenzene.

ε_{ion} = 14,500 ; ε_{base} = 1,440 ; pK_a = -12.15 ; H_o = -11.86 (52)

Oleum Strength $\%H_2SO_4$	$\%SO_3$	ε	$\varepsilon_{ion}-\varepsilon$	$\varepsilon-\varepsilon_{base}$	$\log C_B/C_{ion}$	$(\log C_B/C_{ion})^{1.60\%}$	$-pK_a$
101.56	6.93	5780	8720	4340	0.303	0.293	12.153
101.66	7.37	5900	8600	4460	0.285	0.300	12.160
101.60	7.11	5850	8650	4410	0.292	0.292	12.152
101.57	6.98	5790	8710	4350	0.302	0.294	12.154

TABLE 10. Influence of F_D of Solvent on the Acidity Function.

$\varepsilon_{ion} = 14{,}500$; $\varepsilon_{base} = 1{,}440$; $pK_a = -12.15$ (52)

Oleum Strength %H_2SO_4	%SO_3	ε	$\varepsilon_{ion} - \varepsilon$	$\varepsilon - \varepsilon_{base}$	$\log C_B/C_{ion}$	$(\log C_B/C_{ion})^{1.60\%}$	F_D	$-H_o$
101.65	7.33	6190	8310	4750	0.243	0.256	24.0	11.89
101.71	7.60	6300	8200	4860	0.227	0.254	23.8	11.89
101.66	7.37	6410	8090	4970	0.211	0.226	47.5	11.92
101.60	7.10	6570	7930	5130	0.189	0.189	72.4	11.96
101.59	7.06	6985	7515	5545	0.132	0.130	99.7	12.02
101.64	7.29	6950	7550	5510	0.137	0.147	99.7	12.00

TABLE 11. Influence of the Deuterium Content of the Medium on the Rate of Sulphonation of p-Tolyltrimethylammonium Methosulphate

Oleum Strength		F_D	k_H	k_D	k_D/k_H	
$\%H_2SO_4$	$\%SO_3$		(min^{-1})	(min^{-1})		
101.61	7.15	99.7	0.155	0.121	0.78	0.75
101.64	7.29	99.7	0.173	0.124	0.72	
101.50	6.66	72.7	0.090	0.083	0.92	
101.55	6.88	72.6	0.120	0.113	0.94	0.92
101.66	7.37	72.3	0.185	0.168	0.91	
101.53	6.80	48.0	0.107	0.107	1.00	0.97
101.63	7.25	47.6	0.167	0.157	0.94	
101.65	7.33	24.0	0.179	0.180	1.01	0.98
101.71	7.60	23.8	0.215	0.204	0.95	

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Fig 3. Freeze Drying Apparatus Scale 1" = 2·5" app.

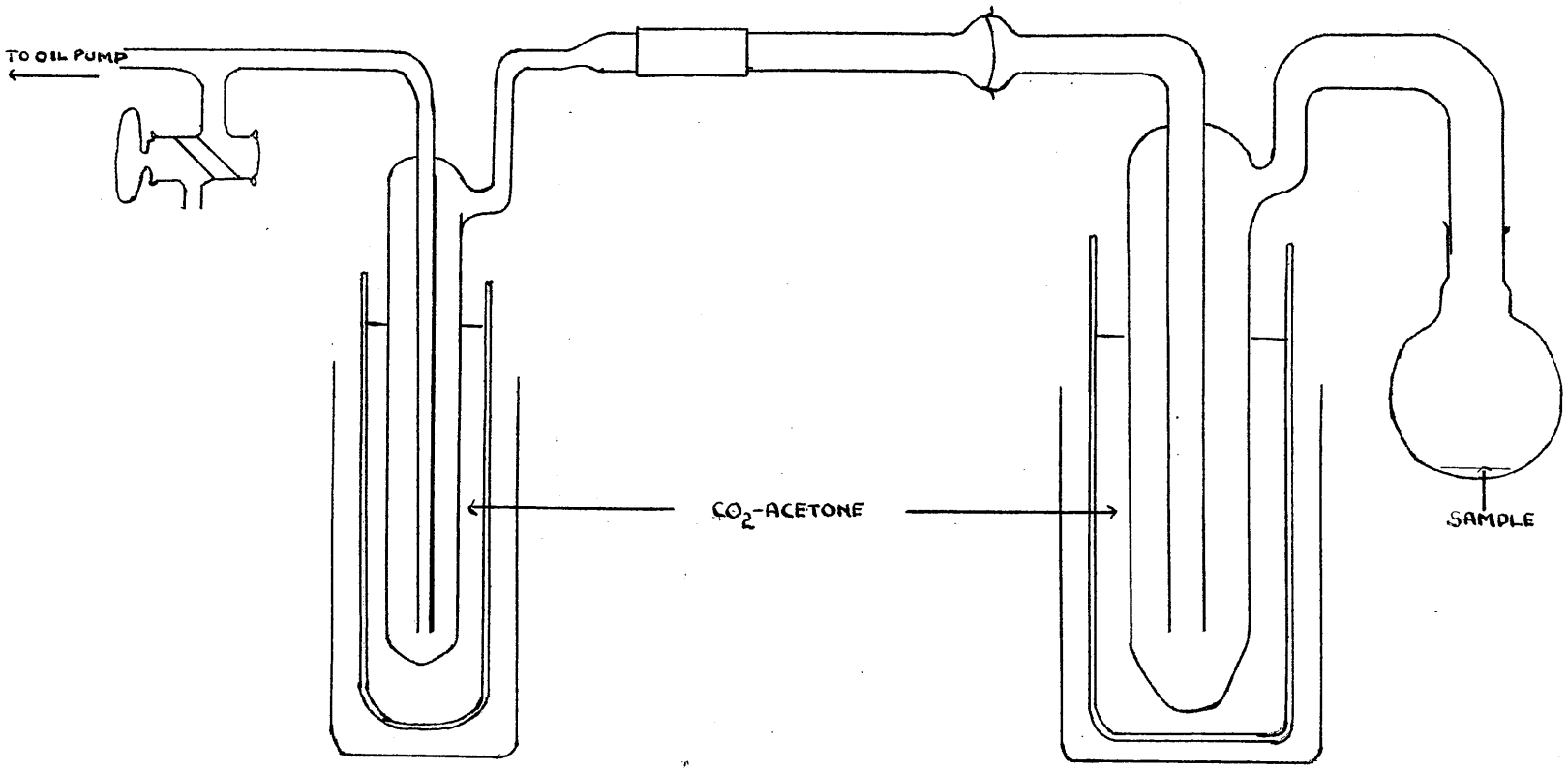

Fig 4. Combustion Apparatus

Scale 1" = 5" app.

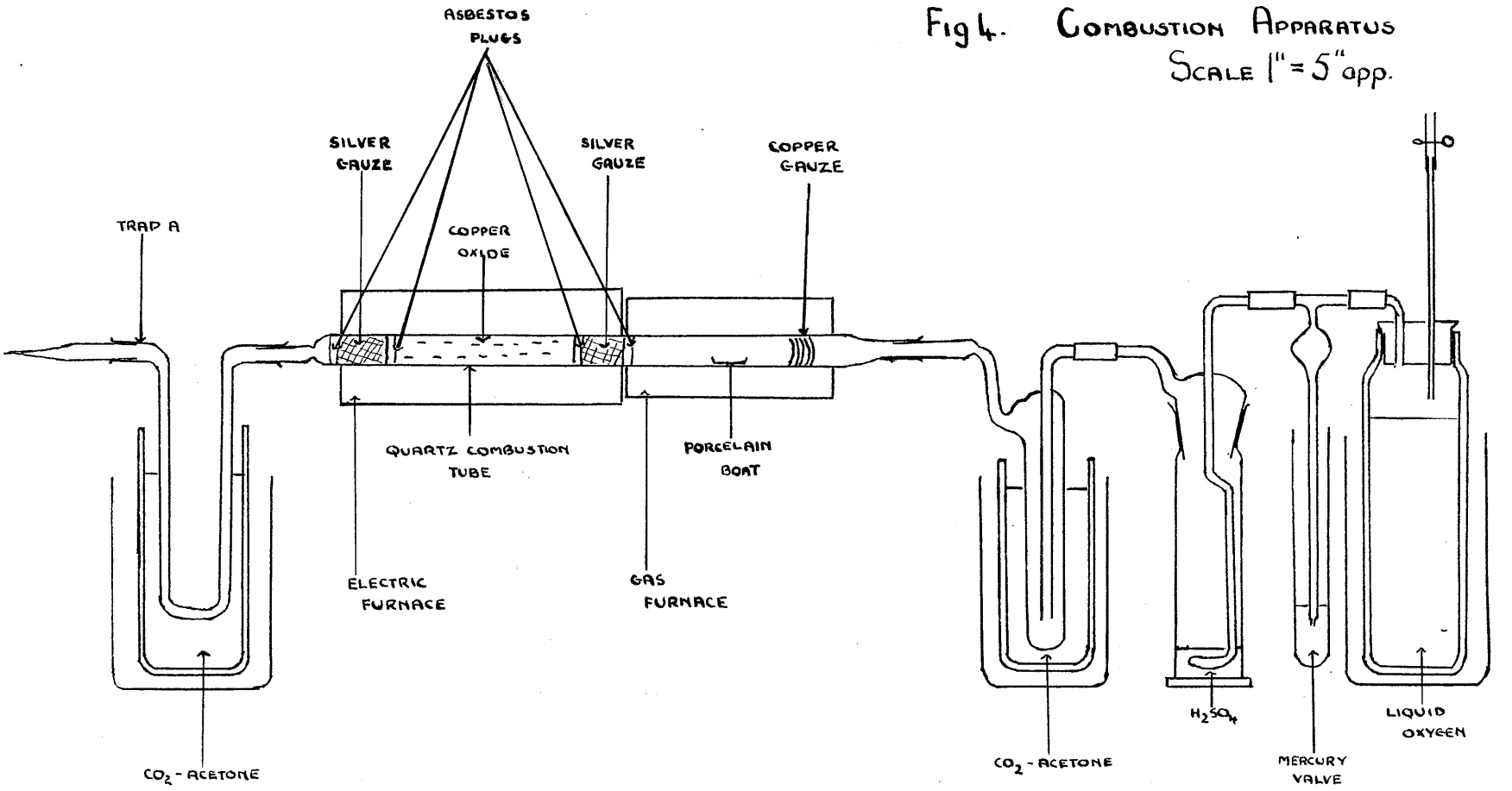

Fig 5 Distillation Apparatus Scale 1" = 5" app.

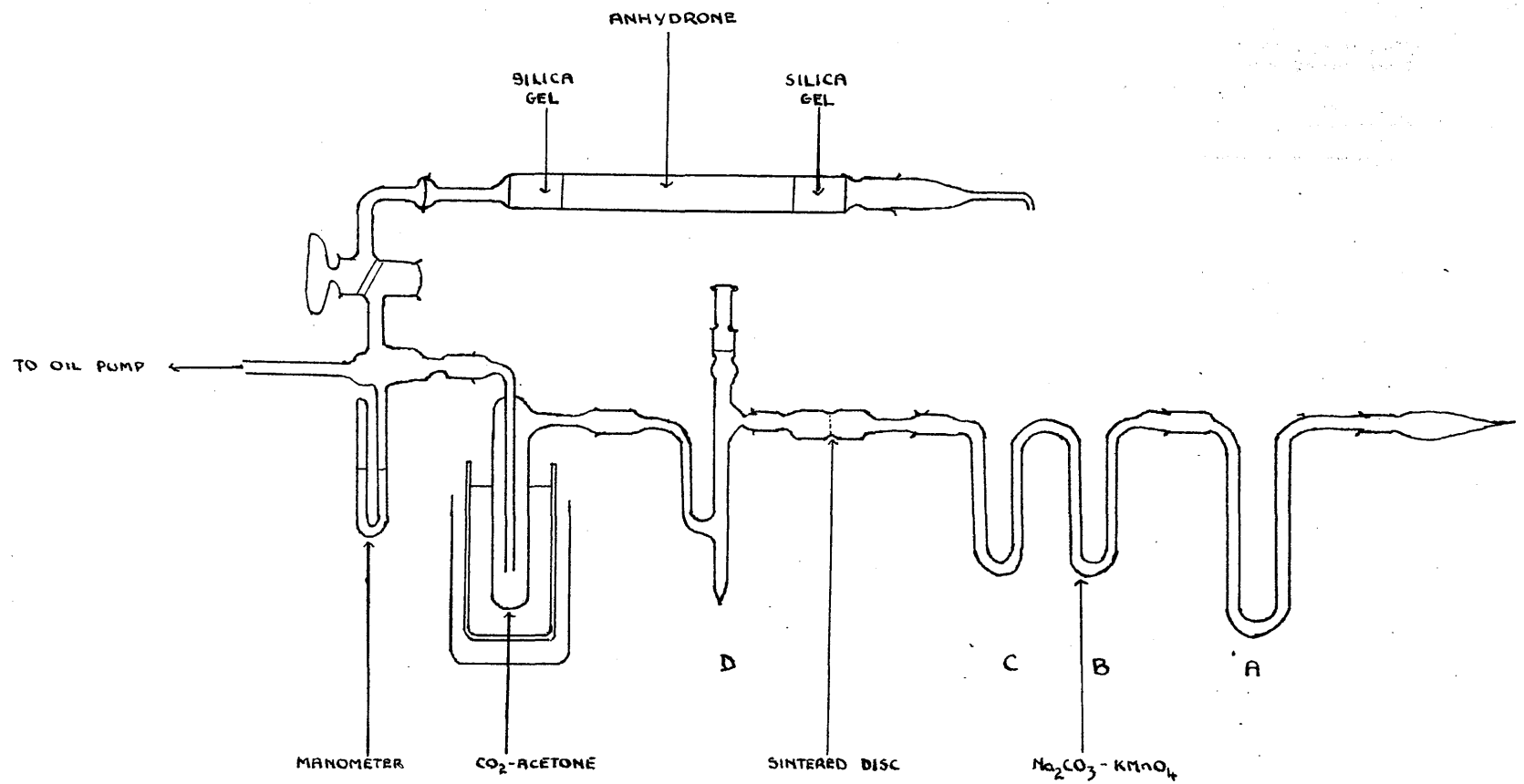

Fig6 PREPARATION OF PURE D_2SO_4

SCALE 1" = 2·5" app.

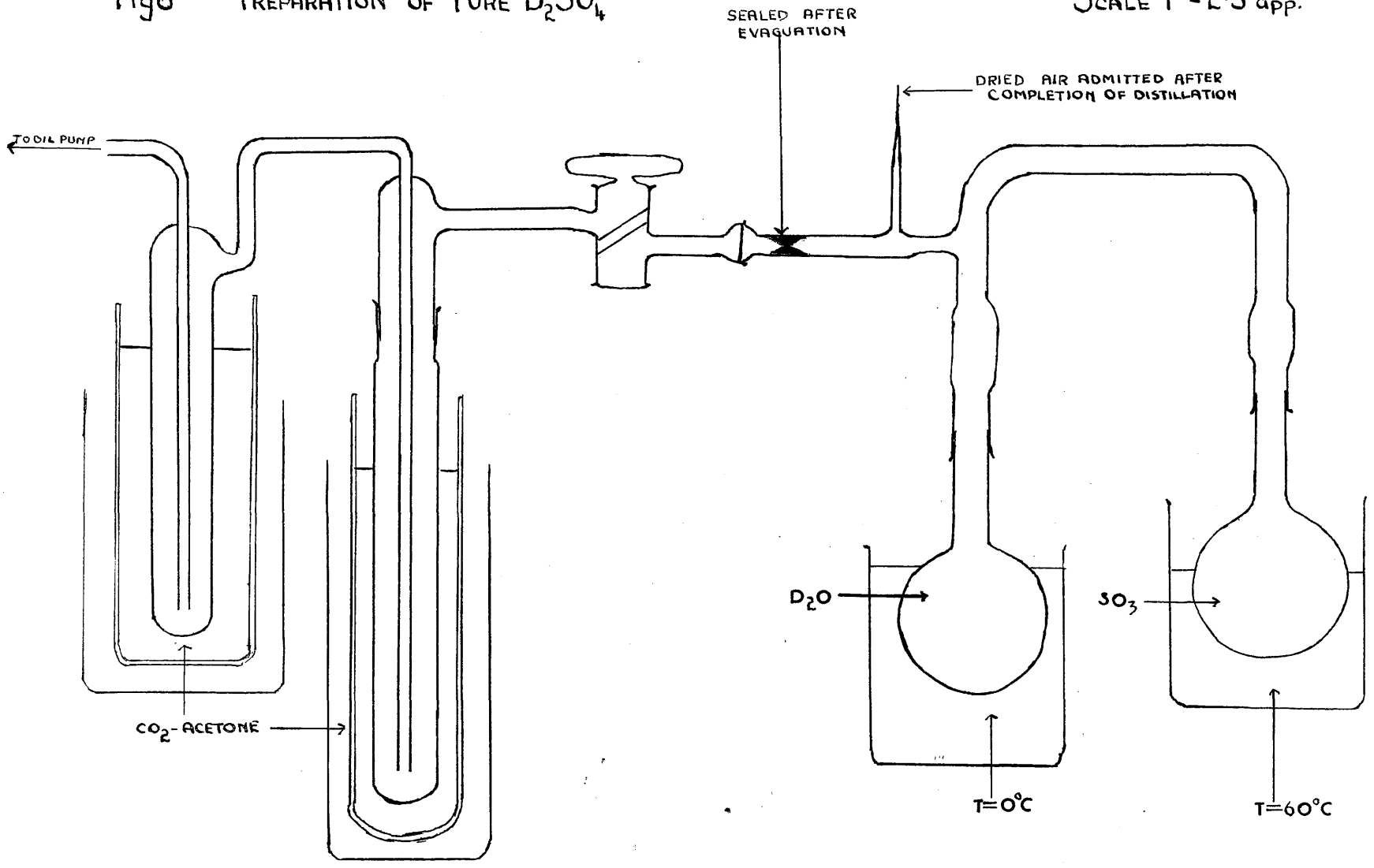

Fig 7

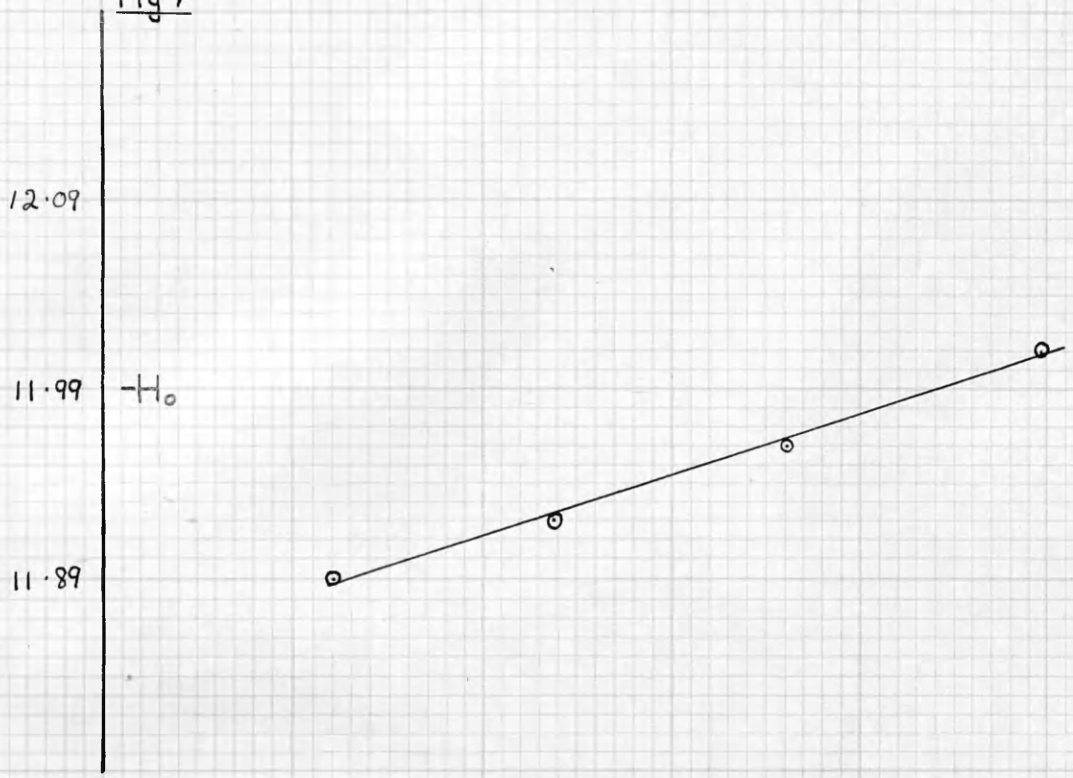

Fig 8